



# ARCHIVES OF SURGERY

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# ARCHIVES OF SURGERY

VOLUME 17

JULY, 1928

NUMBER 1

## BILIARY INTESTINAL ANASTOMOSIS FOR OBSTRUCTIVE JAUNDICE

ANALYSIS OF ONE HUNDRED AND THIRTY-SEVEN CONSECUTIVE CASES \*

E. STARR JUDD, M.D.

AND

BENNETT R. PARKER, M.D.

ROCHESTER, MINN.

We have studied 137 consecutive cases in which anastomosis of the biliary and the gastro-intestinal tracts was carried out at the Mayo Clinic from 1919 to 1924 inclusive. We wished to ascertain, if possible, the end-results of these operations and any other related data which might be correlated and used in the interpretation of the clinical and pathologic manifestations of the various lesions. Obviously, in such a series there are many complications, great technical difficulties and a high mortality rate. The malignant cases were hopeless and the patients were usually in extremely poor general health when they presented themselves for treatment. Many of them were jaundiced and had had previous operations, some of which had caused their chief complaint, as for example, strictures. All were poor risks and required heroic measures for cure, or even for some degree of relief.

Every patient with jaundice, or who had recently been jaundiced, was observed in the hospital before operation. A diet high in carbohydrates was given, fluid was forced, and calcium chloride was administered intravenously. The coagulation and calcium time of the blood were estimated, the serum bilirubin was determined, and tests of hepatic function were carried out if indicated, as well as other special tests which might have direct bearing on the case. As soon as the serum bilirubin dropped to within normal limits and the patient's condition permitted it, operation was performed. In many cases, however, the serum bilirubin did not drop and surgical intervention was imperative, so the risk was accepted and the operation performed.

A review of results in individual cases was not encouraging, but by studying the series as a whole and noting the progress of the various groups, we found that the end-results were better than we had anticipated in cases in which there was even a reasonable chance of improvement or cure.

\* From the Division of Surgery, Mayo Clinic.

For purposes of comparing malignant and benign lesions, the cases were divided into series: (1) carcinoma of the pancreas, thirty-four cases; (2) carcinoma of the ducts, nine cases; (3) carcinoma or pancreatitis, fourteen cases; (4) pancreatitis, eleven cases; (5) stenosis of the bile ducts, sixty-two cases; (6) intrahepatic jaundice (biliary cirrhosis), four cases, and (7) miscellaneous, three cases (one congenital absence of the common duct, one perforating duodenal ulcer causing obstruction of the duodenum and common duct, and one painless jaundice without demonstrable cause). For obvious reasons cases of the same series in which some condition is common to all will be compared.

TABLE 1.—*Carcinoma of Pancreas (First Series)*

	Patients	Percentage	Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice			Patients Surviving Operation		Average Postoperative Life of Patients Now Dead, Months
			Average	Oldest	Youngest	Average, Months	Longest, Years	Shortest, Months	Average, Months	Longest, Months	Shortest, Weeks	No Jaundice	Intermittent	Constant	Not Heard From	Heard From	
Group 1: Colic alone	12	25.59	55.3	70	34	34.25	10	0.5	7.3	48	2	..	5	7	..	4*	0.7
Group 2: Pain alone	8	23.52	59.2	72	49	12.5	5	10	1.5	3	1	1	1	6	2	2†	0.5
Group 3: No colic or pain.....	13	38.23	50.9	61	42	3.5	0.53	0.5	1.5	3	2	..	..	13	2	5‡	4.6
Group 4: Both colic and pain...	1	2.94	67	..	..	60	..	....	0.75	..	..	..	..	1	..	1§	7

\* Two lived six months, one nine months, and one eighteen months.

† One lived four months, and one fifteen months.

‡ One lived three months, one four months, two five months, and one six months.

§ Lived seven months.

#### CARCINOMA OF THE PANCREAS (FIRST SERIES)

This series of thirty-four cases is subdivided into four groups (table 1). In group 1 were twelve cases (35.29 per cent) in which colic without pain was the chief symptom as distinguished from pain with or without jaundice; in group 2, eight cases (23.52 per cent) in which there was pain without colic; in group 3, thirteen cases (38.25 per cent) in which there was neither pain nor colic, and in group 4, one case (2.94 per cent) in which there was both pain and colic. In the past it has been generally accepted that "painless" jaundice signifies a malignant condition. In this series of proved carcinoma of the pancreas, there was a history of pain, colic or both, in 61.75 per cent, while in only 38.25 per cent there was no pain or colic.

In the first group the symptoms had been present nearly three times as long as in the cases in which there was pain alone (second group), and ten times longer than in the group in which there was no pain or

colic (third group). In the first group the average duration of jaundice was seven and three-tenths months, and in the other two groups only one and five-tenths months. Intermittent jaundice was common in the first group in five of twelve cases, it was uncommon in the second group, and in the third, constant. The average length of life after operation in the first group was nine months, in the second group nine and five-tenths months, but in the third, only four and six-tenths months.

Life expectancy in the first group was definitely longer than in the other groups. It was shortest in the third group; in the second it was between the first and the third. This is interesting in view of Judd and Hallberg's report on the results of cholecystectomy in cases of cholecystitis graded 1 and 1—. They found that patients presenting histories of colic and pain alone were cured or improved more often by removing the gallbladder than were those whose predominating complaint was dyspepsia without pain or colic. Seventy-eight per cent of patients suffering from abdominal colic, and 91.2 per cent from typical biliary colic were either cured or greatly improved by removal of the gallbladder, and only 53.6 per cent with a history of dyspepsia without colic or pain were cured or improved. These data are mentioned because of their apparent prognostic value. A stretch of the imagination may be required in order to compare cholecystitis to carcinoma of the pancreas; the comparison is made more for the purpose of calling attention to the relationship than for the purpose of drawing conclusions.

The history extending over many months which is elicited in certain cases of carcinoma of the pancreas may be interpreted as due to a lesion in the biliary tract, even though in most cases such a lesion is not found at the time of the operation; we are, instead, dealing with recent manifestations of what probably is an entirely new entity, the earlier symptoms possibly being due to an infective process in the biliary tract with periods of remission, a point strikingly brought out in cases of true pancreatitis. Possibly true pancreatitis exists before the malignant change, which would explain the relatively long duration of symptoms. It does not seem likely that carcinoma could have existed from the beginning of symptoms.

It will be noticed that age incidence and average life expectancy after operation are essentially the same in three groups, though slightly shorter in the group without pain or colic. The relation of the predominating symptoms, pain and colic, to the length of the history and the duration and type of the jaundice, is worthy of attention, but the end-results in all the groups are the same, as would be expected in cases proved to be malignant.

Jaundice, pruritus, purpura and hemorrhage make the life of these patients distressing, and although they cannot be cured something can be done, such as adequate drainage to relieve the intolerable symptoms. If there is biliary obstruction due to carcinoma of the pancreas, the most



logical procedure is some type of anastomosis between the biliary and gastro-intestinal tracts, thus providing long and adequate drainage and at the same time preserving the bile. The jaundice will disappear and the patient's last days will be spent in comparative comfort. This type of operation is, of course, wholly palliative, and yet occasionally in a case which appears to be carcinoma of the pancreas, cholecystogastrostomy or some such type of operation will result in cure. In such cases it must be assumed that the condition was chronic pancreatitis and not carcinoma. In certain cases it is extremely difficult to determine definitely whether the presenting lesion is carcinoma or pancreatitis, but the operative treatment is the same. Reference will be made to this again in the series, carcinoma or pancreatitis. Surgically, anastomosis is justifiable in all cases of carcinoma of the pancreas in which there is a reasonable chance that the patient may survive the operation. It prolongs the patient's life and relieves him of much suffering.

In this series, besides the original pancreatic lesion, biliary cirrhosis was marked in twelve cases (35.29 per cent), dilatation of the gallbladder in twenty-five (73.52 per cent), dilatation of the common duct in sixteen (47 per cent), enlarged regional lymph nodes in seven (20.5 per cent), hepatitis in one (2.9 per cent), ascites in four (11.7 per cent), metastasis to the liver in five (14.7 per cent), metastasis to the lungs in one, dilatation of the duodenum in one, extension of the process into the duodenum in one, duodenal ulcer in one, and postoperative biliary fistula in one. Gallstones were found in only one case; in one case gallstones had been removed from the biliary tract at a previous operation.

Operations had previously been performed on the biliary tract in five cases (14.7 per cent). The gallbladder had been drained in two cases one year and one month before, respectively, with only short periods of relief; stones were not found in either case. The gallbladder and common duct had been drained for stones in one case, with relief for two years, and in another, the gallbladder which did not contain stones had been removed, without improvement. In the fifth case the gallbladder had been anastomosed to the stomach three months previously, with relief for two months; recurring symptoms were due to contraction of the stoma. The anastomosis was reconstructed and the stoma enlarged.

Cholecystogastrostomy was performed in twenty-six of the thirty-four cases, cholecystoduodenostomy in four, cholecystojejunostomy in two, choledochoduodenostomy in one case and cholecystocolostomy in one. Much has been written concerning ascending infection by way of the stoma and lymphatics. Experimentally, infection or irritation is easily demonstrated in almost all cases in which the gallbladder is anastomosed to the intestinal tract. As would be expected, the infection is greatest when cholecystenterostomy or cholecystocolostomy is performed and much less when the anastomosis is with the duodenum or

stomach. Cholecystenterostomy or cholecystocolostomy is never performed save when it is impossible to utilize the stomach or duodenum, and in these cases the operation is for palliation and there can be no choice of method. It is expected that infection will result from direct extension or by the periductal lymphatics; this would not be likely to occur within the life expectancy period. The usual result of such infection probably is hepatitis and some degree of cholangitis, both of which are of secondary importance in the presence of carcinoma of the pancreas and other conditions which preclude the possibility of utilizing the stomach or duodenum in the anastomosis. In this series, there does not appear to have been a choice of operation. Obviously, high anastomosis should always be done if possible, regardless of the type of lesion.

One of the patients in this series who survived operation lived eighteen months; one, fifteen months; one, nine months; one, seven months; two, six months; one, five months; two, four months, and one, three months. Four were not heard from. We do not have any information concerning the details of one patient's life after he left the clinic. One of the remaining eleven patients had slight jaundice associated with mild attacks of dyspepsia, and three others had jaundice with pain and chills and fever coming on shortly before death. The remaining seven patients were free from jaundice, but four of these had had occasional attacks of dyspepsia with gas and bloating. All failed progressively. One patient died at home; necropsy confirmed our diagnosis of carcinoma of the pancreas.

Colic with jaundice occurred in 35.29 per cent of the cases, pain with jaundice in 23.52 per cent, and colic, pain and jaundice in 2.94 per cent. Thus colic or pain or both with jaundice occurred in 61.75 per cent and "painless" jaundice on only 38.23 per cent. The life expectancy after operation in cases in which there was pain or colic or both was twice as long as in those in which pain and colic were absent. The average postoperative life expectancy in all groups was seven and seven-tenths months. The relief from jaundice of patients surviving operation was complete and permanent in 63.63 per cent.

The types of anastomosis were not sufficiently varied so that conclusions could be drawn with regard to the type giving the best results, and the postoperative life of the patients was too short to make such evaluation.

#### CARCINOMA OF THE BILE DUCTS (SECOND SERIES)

The nine cases in this series (table 2) were grouped, as in the first series, with reference to the presenting symptoms. In general, the duration of the disease and the duration and type of the jaundice were similar to the first series. The series is divided into three groups. In group 1 were two cases (22.22 per cent), in which there was colic without pain;

in group 2, four cases (44.44 per cent) in which there was pain without colic, and in group 3, three cases (33.33 per cent) in which there was neither pain nor colic. In the first group the history was almost eight times longer; the type of jaundice was more varied but unlike that in the first series, the average duration of jaundice was approximately as short or shorter than in the second and third groups. In the second group the average duration of symptoms was shorter and the jaundice more often constant, while in the third group the average duration of symptoms was the shortest of all groups and the jaundice was always constant, while the average duration of jaundice was the longest of the three groups.

TABLE 2.—*Carcinoma of the Bile Ducts (Second Series)*

	Patients	Percentage	Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice		Patients Surviving Operation	
			Average	Oldest	Youngest	Average, Months	Longest, Months	Shortest, Months	Average, Months	Longest, Months	Shortest, Months	Intermittent	Constant	Heard From	Average Postoperative Life of Patients Now Dead, Months
Group 1:															
Colic alone	2	22.22	47	51	34	63	63	60	2	3	1	1	1	2*	0
Group 2:															
Pain alone	4	44.44	53.5	61	44	7.7	21	0.75	1.2	3	0.75	1	3	2†	..
Group 3:															
No colic or pain.....	3	33.33	55.0	57	55	0	8	4	4.0	8	2	..	3	1‡	17

\* One lived six months, and one twelve months.

† One was living five months and one twenty-one months later.

‡ Lived seventeen months.

The postoperative life expectancy in these three groups is a trifle longer than in the corresponding groups in the first series. Since there are only nine cases in this series, definite conclusions cannot be drawn, yet the similarity between the two series is close enough to warrant drawing attention to it.

In five of the nine cases the lesion was situated at the ampulla, in one it was low in the common duct, in two in the common duct just below the juncture of the cystic duct; the site of one was not specified. Biliary cirrhosis was present in four cases (44.44 per cent), dilated gallbladder in six (66.66 per cent), dilatation of the common duct in seven (77.77 per cent), ascites in two (22.22 per cent), and metastasis to the liver, enlarged glands, large spleen, and a perforated gallbladder, each in one instance. In only one case was there evidence of disease in the gallbladder, and in this the gallbladder had perforated.

Cholecystogastrostomy was performed in five cases, cholecystoduodenostomy in one case, choledochoduodenostomy in two cases and cholecystojejunostomy in one case.

The five patients who survived operation (three who had had cholecystogastrostomy, one cholecystojejunostomy, and one cholecystoduodenostomy) improved immediately and returned home with the jaundice cleared or clearing. One patient was much improved five months after the operation: he was however, having some dyspepsia and occasional chills and fever, but no jaundice. We have not heard from him during the last eighteen months. Three patients lived seventeen, twelve and six months, respectively. Two were permanently relieved of jaundice and one was completely relieved for a year, when there was recurrence of the former trouble and death occurred seventeen months after operation. In the remaining case, that of a man, aged 44, a history was elicited of typical textbook type of recurring gallstone attacks without jaundice. At operation dilatation of the gallbladder was graded 3, the dilatation of the common duct was graded 2, enlargement of the regional lymph nodes was graded 2, and chronic appendicitis was graded 2: the pancreas, stomach and duodenum appeared normal. Cholecystectomy and appendectomy were performed with relief of symptoms for two months, when constant painless jaundice appeared and lasted three weeks. A second operation was performed three months after the first. At this time dilatation of the common duct with white bile was graded 3, and enlargement of the regional lymph nodes was graded 2: the pancreas appeared normal. A tumor 2.5 by 0.5 cm. at the ampulla projected into the duodenum. Biopsy resulted in a diagnosis of colloid carcinoma. Resection of the ampulla of Vater and choledochoduodenostomy was carried out. The patient returned home with jaundice cleared and a gain of 75 pounds (34.9 Kg.) in weight. Eighteen months after the second operation, symptoms returned and a month later exploration, because of obstructive jaundice, revealed a firm mass involving the second portion of the duodenum. The evidence suggested probable involvement of the retroduodenal lymph nodes, doubtless recurrence of the carcinoma. The patient was now getting along fairly well (two months after the last operation and twenty-one months after the second operation), but complained of weakness. The jaundice had entirely disappeared.

Colic with jaundice occurred in 22.22 per cent of cases, pain with jaundice in 44.44 per cent, and "painless" jaundice in 33.33 per cent. The duration of symptoms was longer in the first group than in the other two groups. Unlike the corresponding groups in the first series, the duration of jaundice was longest in the group without pain or colic, but the type of jaundice was the same as in the corresponding groups:

years and one three years and eight months after operation; one patient, when last heard from one year after operation, had not had jaundice, chills or fever, but had had some dyspepsia and constipation. Three patients consider themselves cured, and one considers himself much improved.

One patient had had pain without colic for one year and constant jaundice for six months; an operative diagnosis of carcinoma of the pancreas, 95 per cent, and pancreatitis, 5 per cent, was made. After cholecystoduodenostomy was performed, the patient went home much improved. One year later he considered himself cured, and six years later he is well and living a normal life. This is an instance which exemplifies the value of operative treatment in these indefinite cases. Such a striking example of cure of an apparently hopeless condition emphasizes the desirability of rather heroic treatment. If the condition proves to be carcinoma, the patient has at least been relieved of jaundice and made fairly comfortable. If, however, the condition proves to be a benign lesion, great improvement or even cure may be expected.

In cases in which it is impossible definitely to differentiate carcinoma or an inflammatory process, anastomosis of the biliary tract to the intestine is a logical procedure. Such an operation may be considered an "operative, therapeutic test." If the patient is cured or improved and lives longer than the life expectancy for carcinoma of the pancreas, it may be assumed that the condition is pancreatitis, while if the patient survives the operation and dies within the life expectancy period, it may be assumed that the lesion was malignant and not pancreatitis. This may appear unscientific, but it is justified clinically by the results obtained. If the patient dies, apparently from carcinoma, the operation must be considered as palliative only. The average length of life after operation of patients who died was nineteen and six-tenths months.

The history-jaundice ratio in the first group of the third series is entirely unlike that in the first and second series.

#### PANCREATITIS (FOURTH SERIES)

There were eleven cases in this series. These cases cannot be separated according to the groups as in the three former series. In the first group were six cases in which there was a history of colic or pain, but the distinction was not clear and in the second were five cases in which there was neither pain nor colic (table 5).

In the first group the duration of symptoms averaged five and two-tenths years, in the second it averaged only ten and six-tenths months. The type and duration of jaundice in the two groups were the same, the intermittent jaundice being somewhat more common in the first group, similar to that in the corresponding groups of the previous three series.

The associated lesions were about the same in the two groups, but with the difference that the regional lymph nodes were greatly enlarged in three cases in the first group and in only one in the second group; the gallbladder was markedly dilated in four cases in the second group and in only one in the first group. Cirrhosis was specified in five cases (45.45 per cent), stone in the common duct in one case (9 per cent), dilated common duct in two cases (18.18 per cent), gallstones in one case (9 per cent), hepatitis in four cases (36.27 per cent), large spleen in two cases (18.18 per cent) and ascites in one case.

In two cases an operation had previously been performed on the biliary tract. In one case, cholecystostomy had been performed with seven months' relief, and in the other, cholecystostomy two years previ-

TABLE 5.—*Pancreatitis (Fourth Series)*

	Patients	Percentage	Age, Years			Duration of Symptoms			Duration of Jaundice			Type of Jaundice		Patients Surviving Operation	
			Average	Oldest	Youngest	Average, Months	Longest, Years	Shortest, Months	Average, Months	Longest, Years	Shortest, Months	Intermittent	Constant	Heard From	Average Postoperative Life of Patients Now Dead, Months
Group 1: With pain and colic....	6	54.54	37.5	55	20	62.4	28	0.75	10.3	1.25	0.75	4	2	6*	3
Group 2: No pain or colic.....	5	45.45	41.4	57	18	10.0	2	3	14.8	2	3	2	3	2†	9.5

\* One was living two years later, one one year, one fourteen months, and one three years; one lived five years and one three months.

† One lived one and a third year and one three months.

ously had resulted in biliary fistula for one year. Cholecystoduodenostomy was then performed, with relief for one month. At the last operation the stoma was found to be completely closed and it was reconstructed over a tube.

Cholecystogastrostomy was performed in seven cases, cholecystoduodenostomy in three, and cholecystoduodenostomy and splenectomy in one case. All of the patients in the first group lived to go home. One died three months after operation, probably from carcinoma of the pancreas. The jaundice had been completely relieved. One patient died five years after operation from cerebral hemorrhage; he had been completely cured of his former trouble. Four others considered themselves cured three years, two years, one year and two months, and one year, respectively, after operation.

It is impossible to draw conclusive deductions from such a small series of cases. Yet, in the light of the three previous series, the prog-

nosis in the group presenting colic and pain is better than in that in which colic and pain were absent. The postoperative results in the first group were much better than in the second, which is entirely in keeping with the data in the corresponding groups of the first three series of cases.

There is a consistent prognostic relationship in the corresponding groups of all the series in regard to the cases presenting symptoms of colic or pain, as compared with those without pain or colic. In a large percentage of cases of a malignant condition in the pancreas or ducts and of carcinoma of the pancreas or pancreatitis there was jaundice with pain or colic, so that the "painless" type of jaundice cannot hold the same diagnostic importance as formerly, but the dilated gallbladder of Courvoisier's law can be accepted as a presumptive sign of carcinoma (table 6). In obstructive jaundice due to stenosis at the ampulla, inflammatory reactions of the pancreas, carcinoma, cicatrix and calculus must be considered. It is usually fairly easy to distinguish the latter, but in the other cases accurate differential diagnosis is often impossible. In the doubtful cases we have felt that exploration of the pancreas is not without danger, and on that account biopsy has been done in only a few cases. Doubtless biopsy is justifiable and is of great value if it can be done without adding to the great risk already accepted in performing an operation. Without biopsy, gross examination of the organ must be relied on. In carcinoma of the pancreas, the local reactions are usually less than in the inflammatory lesions, and the tumor is more easily felt as an extremely hard and indurated mass with adenopathy characteristically different from that in chronic inflammation. Too much significance cannot be placed on the presenting symptoms in making a differential diagnosis, because on analysis it will be found that in a high percentage of malignant cases the presenting symptoms will be colic and pain, as well as jaundice (table 4). The treatment in cases of obstructive jaundice consists in the relief of biliary retention, the treatment of the pancreatic lesion, and the treatment of the cause of the pancreatic lesion. The simplest operative technic which will warrant cure or relief from jaundice as a palliative measure is the best. Exploratory operation is sometimes necessary to establish a diagnosis. If carcinoma is present, a palliative operation is performed. If the condition is benign, jaundice should be relieved and some type of good biliary drainage instituted. In the benign conditions, from a pathologic point of view, cholecystostomy or cholecystectomy is the logical procedure, since it is believed that the original focus is in the gallbladder in a large percentage of cases. Removal of the gallbladder, however, does not relieve the patient from jaundice; thus a dangerous situation is brought about, for at some future time the gallbladder may be needed for an anastomosis to cause relief from jaundice. Cholecystostomy probably is the simplest opera-

tive treatment, but the drainage is not reliable; it is irregular and the fistulous tract may close too soon and cause a return of symptoms, or it may persist after the pancreatic lesion has been apparently cured. Also the bile is lost to the patient, which is serious in long-continued drainage. While the establishment of internal biliary fistula requires more operative procedures, it is probably desirable since long-continued drainage is secured and the bile is preserved for the patient's use, provided the anastomosis is not made with the colon. We have already mentioned the unexpected cure of an apparently hopeless condition by anastomosis of the biliary and intestinal tracts. In the doubtful case, in which a tentative diagnosis has been made, the internal biliary fistula is probably the best operative treatment, be it palliation for carcinoma, or a curative measure for pancreatitis.

In the cases in which cholecystogastrostomy has been performed for benign lesions, such as pancreatitis, the presence of bile in the stomach does not cause disturbance of digestion, as is commonly believed. Gastric

TABLE 6.—*Cases with Dilatation of the Gallbladder and Common Duct*

Series	Cases	With Dilatation of Gallbladder		With Dilatation of Common Duct	
		Cases	Percentage	Cases	Percentage
Carcinoma of pancreas.....	34	25	73.52	10	46
Carcinoma of ducts.....	9	6	66.66	7	77.77
Carcinoma of pancreas or pancreatitis.....	14	12	85.71	8	57.14
Pancreatitis .....	11	5	45.45	2	18.18

analyses following these operations consistently show bile in the gastric content and always some acid, combined and free, but in less than normal amounts. Anacidity which one might expect, is rarely found. Physiologically, from eight to ten times the twenty-four hour secretion of bile would be necessary to neutralize the secretion of the stomach for a like period, not taking into account the digestion of protein foods. In many instances, if an anastomosis has been made over a rubber tube the patient complains of "dyspepsia" until the tube has passed, and after this he is completely relieved of the digestive disturbance. A woman in whom hepaticoduodenostomy was made over a rubber tube had dyspepsia for twenty-two months. After the tube was passed, she was completely free from symptoms.

#### STENOSIS OF THE BILE DUCTS (FIFTH SERIES)

There were sixty-two cases of stenosis of the bile ducts in which a reconstruction operation was inadvisable or impossible because of the destruction or absence of the necessary structures. With one exception, operation had been performed previously on the biliary tract; in some cases multiple operations had been performed. The one exception was



that of a case in which there was a three-year history of recurring attacks of typical biliary colic, recently with questionable jaundice. The last attack was extremely acute and at the time of operation acute cholecystitis (graded 3) with stones was found. The common duct was densely adherent to the gallbladder, forming an extensive cicatricial stricture and an acute angulation of the duct. Dense adhesions were present in the regions of the gallbladder and duct. Any type of reconstruction operation would have been a failure, so the gallbladder was excised and hepaticoduodenostomy performed. The immediate results were good and six years after the operation the patient was living a normal life, with slight abdominal pain and jaundice at rare intervals, but the symptoms were not severe enough to cause him to consult a physician.

In five of the remaining sixty-one cases, cholecystostomy alone had been performed previously with an average of fifteen and six-tenths months' relief from symptoms. In twenty-seven, cholecystectomy had been performed with an average of two and four-tenths months' relief. There were twelve cases in which cholecystostomy and cholecystectomy had been performed at different times, with an average period of relief of symptoms after cholecystectomy of seven and three-tenths months. In four cases, in which the gallbladder had been removed and the common duct drained at the same time, the average period of relief was three and two-tenths months. In six cases in which cholecystectomy and drainage of the common duct had been performed at different times, the average period of relief after the last operation was two and six-tenths months. There were seven other cases in which there had been two or more operations at different times before the patients presented themselves at the Mayo Clinic (table 7). The primary operation was cholecystectomy in forty-three cases and cholecystostomy in eighteen.

It was noted that trouble appeared immediately after the primary operation in certain cases, while in others there was no evidence of trouble for some time afterward. In certain cases the stricture was probably the result of trauma at the time of the operation, while in other cases it was undoubtedly due to a continuation of the inflammation in the bile ducts, which finally resulted in obliteration. Many cases attributed to trauma are due to obliterative cholangitis. In thirteen cases persistent biliary fistula followed cholecystectomy: in one it followed cholecystostomy, and in five it followed drainage of the common duct. Persistent biliary fistula following cholecystectomy or drainage of the common duct is probably the direct result of injury to the duct at the time of the first operation, which emphasizes the responsibility a surgeon assumes in performing even simple cholecystostomy or cholecystectomy.

Pain and colic were common to all cases in this series. In only three was there no definite jaundice; in all the others intermittent jaundice of some degree was present. In those with biliary fistula, the pain, chills, fever and jaundice were the direct result of the inadequate drainage.

The various types of operations were hepaticoduodenostomy in forty-seven cases, hepaticogastrostomy in two, cholecystogastrostomy in one case, cholecystoduodenostomy in two cases, choledochoduodenostomy in seven, hepaticocholedochostomy in one case, and choledochhepaticoduodenostomy in two cases.

Eight patients died at home. The one who survived longest lived four and a half years after operation, apparently cured, then died from

TABLE 7.—*Stenosis of Bile Ducts (Fifth Series) Previous Operations; Sixty-One Cases (98.38 Per Cent)*

Patients	Previous Operations	Average Period of Relief From Symptoms After Last Operation, Months*	Longest Period of Relief, Months	Shortest Period of Relief, Months
5	Cholecystostomy .....	15.6	24	2
27	Cholecystectomy .....	2.4	9	None
12	Cholecystostomy and cholecystectomy.....	7.3	36	None
4	Cholecystectomy and choledochostomy at same time..	3.2	6	1
<b>Multiple Operations at Different Times</b>				
6	Cholecystectomy and choledochostomy.....	2.0	2	None
1	Cholecystostomy; cholecystectomy; choledochostomy..	6	..	..
1	Cholecystectomy; second operation for "adhesions"...	1	..	..
1	Cholecystectomy; operation for "adhesions"; hepaticoduodenostomy; reconstruction of stoma.....	2	..	..
1	Cholecystectomy; reconstruction of common duct.....	None	..	..
2	Choledochostomy; cholecystectomy; hepaticoduodenostomy .....	3.5	4	3
1	Choledochostomy; cholecystectomy; dilatation of stricture of common duct .....	None	..	..

\* Average relief after last operation for all cases, four and seven-tenths months.

acute gastric obstruction which had required gastro-enterostomy. The patient who survived the shortest time lived ten months. In this case there had been a gradual return of symptoms, and death was due to "starvation." The average length of life of these eight patients was twenty-nine and six-tenths months. In all cases the immediate post-operative results had been good, with recurrence of symptoms and gradual failure. Three of the eight patients were jaundiced shortly before death, and two were mildly jaundiced at intervals after the operation.

Seventeen patients consider themselves cured at periods of from one to five years after operation, the average being one and seven-tenths years. Sixteen patients were greatly improved at periods ranging from two to six years after operation, the average being four years. They complain of infrequent mild attacks of abdominal pain without jaun-

dice; mild dyspepsia was mentioned occasionally. They are living normal lives, and working; they do not require the services of a physician. Nine patients are in fair health only. This means that they have more attacks of abdominal pain with or without jaundice. Two patients have had occasional attacks of pain, chills, fever and jaundice, but little dyspepsia. They are, however, living fairly comfortably, with one exception, a man, aged 61. Two patients (4.8 per cent) have not been heard from.

#### INTRAHEPATIC JAUNDICE (SIXTH SERIES)

In the four cases of biliary cirrhosis in this series, cholecystogastrostomy had been performed. The average history was of ten months' duration. Jaundice was constant and the average duration was nine and seven-tenths months. In each instance, besides definite and marked cirrhosis, the regional lymph nodes were markedly enlarged. An operation had been performed previously on only one case. The gallbladder had been drained and stones removed fourteen years before, with complete relief until one month before the patient presented herself for treatment. The immediate results were good, and one and a half years after operation she was much improved, but occasionally experienced slight jaundice and mild dyspeptic attacks in which "gas" was a prominent symptom. The three remaining patients have not been heard from.

#### MISCELLANEOUS (SEVENTH SERIES)

There were three cases in this series: congenital absence of the common duct; obstruction of the common duct and duodenum due to perforated duodenal ulcer, and jaundice from undetermined cause.

The first case was that of a baby girl, aged 5 months, who had been jaundiced since birth. There was general adenopathy and the liver and spleen were much enlarged. At operation the gallbladder was found buried in the liver and the common duct extended only to the gallbladder. There was a moderate amount of free bile-stained fluid in the abdomen and the liver and spleen were large. The side of the gallbladder and the common duct were anastomosed to the duodenum. The child died three days after the operation. At necropsy no connection was found between the bile ducts and the duodenum. The duct ended as a blind pouch; it was this pouch which had been anastomosed to the duodenum. There was cirrhosis of the liver, graded 1, and hypertrophy of the spleen. The cause of death was peritonitis and pneumonia.

In the second case, that of a woman, aged 49, there had been typical recurring attacks of biliary colic with nausea and vomiting, but without jaundice for six years. Two years previously the gallbladder had been drained, with relief for six months. Then a biliary fistula developed,

with return of the former symptoms. At operation, a large perforating duodenal ulcer was found which had caused marked deformity with obstruction of the duodenum and the common duct. The gallbladder was small and showed evidence of chronic cholecystitis. The stomach was moderately dilated. The biliary fistula was excised, and cholecystoduodenostomy and posterior gastro-enterostomy were performed. The patient recovered uneventfully and six years after the operation considered herself completely cured.

In the third case, that of a man, aged 62, indefinite dyspepsia had existed for four years, and six weeks prior to examination painless jaundice with nausea and vomiting had developed. At the time of operation the dilatation of the common duct was graded 2; stones could not be found. Enlargement of the regional lymph nodes was graded 2. The pancreas and ampulla were normal and the liver was in good condition. No cause could be found for the jaundice and a diagnosis of "jaundice of undetermined origin" was made. Cholecystogastrostomy was performed. The patient recovered uneventfully and left the clinic with the jaundice practically cleared. He returned eight months later with a small ventral hernia, of no consequence, and reported marked improvement. He had not been jaundiced since the operation. Occasionally he had been troubled with slight dyspepsia.

#### SUMMARY OF POSTOPERATIVE RESULTS

In the 137 cases discussed, there were nine of contraction of the stoma. Partial or complete contraction of the stoma occurred in seven of the forty-seven cases in which hepaticoduodenostomy had been performed for stricture. Return of symptoms occurred from one to six months after operation, the average being four and two-tenths months. Reconstruction of the stoma over a rubber tube was carried out in each instance. One patient was apparently cured and died from acute gastric obstruction one and a half years after operation. Five patients are still living from two to four and a half years after operation, the average being two and nine-tenths years. Two of the five have been completely relieved of their former trouble for four and a half and three years, respectively. Three are much improved, but occasionally have slight attacks of pain, chills, fever and jaundice, although not severe enough to require the services of a physician. There were two other cases in which the stoma of the anastomosis contracted and produced obstruction to drainage of bile. In one, cholecystogastrostomy had been performed for obstructive jaundice due to carcinoma of the pancreas. After two months there was a return of symptoms, requiring reconstruction of the contracted stoma. In the other case cholecystoduodenostomy had been performed for obstructive jaundice caused by pancreatitis. Return of symptoms necessitated enlargement of the contracted stoma.

# BLOOD IN THE CEREBROSPINAL FLUID

## RESULTANT FUNCTIONAL AND ORGANIC ALTERATIONS IN THE CENTRAL NERVOUS SYSTEM \*

### A. EXPERIMENTAL DATA

CHARLES BAGLEY, JR., M.D.  
BALTIMORE

This work has been done with the hope of experimentally producing lesions simulating those occurring in human beings when a small amount of blood escapes into the subarachnoid space.

### METHODS AND MATERIAL

Eighteen adult dogs (exact age unknown) and twenty-six puppies (five litters), all less than 10 days old, were injected with whole blood. An average pup from each litter was used as a control.

The whole blood was obtained from the vein in the leg of the adult dogs and from the longitudinal sinus of the pups. Free mixture of the blood and cerebrospinal fluid was desired, and the blood was slowly injected into the cisterna magna, into the subarachnoid space over the cerebral hemisphere and in a few instances, into the cerebral ventricles.

The work was started on adult dogs with frequent injections of from 0.5 to 2.5 cc. of blood. Larger amounts could not be injected into the cisterna magna without causing serious respiratory symptoms, but in a few instances, as much as 5 cc. was tolerated over the cerebral cortex. In the beginning, when adult dogs were being used, it was thought that repeated injections at short intervals would be required to produce a disturbance comparable to that observed in human beings with bloody cerebral spinal fluid; for this reason, some of the earlier dogs received as many as six injections. In the later experiments with young pups, it was found that a single injection would sometimes produce symptoms; therefore, most of these pups received only one or two injections.

Ether anesthesia was used in the adult dogs. Morphine,  $\frac{1}{8}$  grain (0.01 Gm.) was given hypodermically about a half an hour before the administration of ether. Chloroform without morphine was used in anesthetizing the pups.

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\* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, Johns Hopkins University, with the assistance of the Epilepsy Medical Research Fund.

When the animals died or were killed, autopsies were performed. To avoid possible injury of the meninges in the removal of the brain, the skull containing the brain was sectioned with a fine saw and then immersed in 10 per cent formaldehyde. By this method any portion desired for photography or microscopic study could be exposed in the fresh state and the entire brain easily brought into contact with the fixing fluid. The tissue was embedded in paraffin unless the dura was included in the blocks, in which case celloidin was used. Hematoxylin and eosin stain was used.

#### CLINICAL COURSE

Immediately after the injection, the adult animals were restless, spastic and recovered from the narcosis slowly. At times the spastic extremities were active; in some cases, the movements simulated running. At other times, there were atypical convulsive seizures with frothing at the mouth. The day following the injections the animals were usually dull, but walked about the cage and took food. After the injections, the dogs were kept under observation in the laboratory from one to three hours; then they were returned to the animal room. Daily visits were made to the animals, and every few days they were brought into the laboratory and allowed to play about under observation from one to three hours. In this way, it was possible to record symptoms which varied from difference in behavior to severe convulsive seizures.

The clinical course in most of the adult dogs was short because of the brief intervals between the injections. Many of them died within a few days after the last injection with gradually increasing debility marked chiefly by emaciation and irritability. They were hypersensitive and would cry out if handled. One of the adult dogs was given four injections into the cisterna magna over a period of one month, and was kept under observation thirty days after the last injection. During this period, there was gradually increasing weakness; because of the poor physical condition, the dog was killed with chloroform. A section from the base (fig. 3) shows chronic checking.

The most striking clinical course was seen in the younger dogs. This was first noticed in the behavior of the animals that had received injections as compared with the controls. After recovery from the immediate effects of the injection, the pups were less active, so that the puppies that had been treated could be picked out of the litter by the fact that they retired to a corner of the room and showed little of the characteristic tendencies of such animals to play. When stirred to activity, they would lose interest much more quickly than the controls.

In spite of the fact that the puppies ate well, they were generally smaller and markedly thinner. The difference in size between the control animals and animals that had received injections was seen in a



Fig. 1.—*A* indicates the frontal section through the brain of one of the control pups showing the normal ventricle to be very small; *B*, the dilated ventricle of adult dog 10 which received six injections of blood in the cisterna magna over a period of thirty-nine days and was killed two days after the last injection; *C*, the brain of pup 35 which received three injections of blood over the right cortex and two in the cisterna magna over a period of forty-two days and was killed twenty-one days after the last injection; *D*, the brain of pup 37 which received two injections of blood over the right cortex and two in the cisterna magna over a period of forty-two days and was killed seven days after the last injection; *E*, the brain of pup 45 which received one injection of blood in the cisterna magna and was killed twenty-one days later; *F*, the brain of pup 47 which received two injections in the cisterna magna over a period of seven days and was killed ten days after the last injection; *G*, the brain of pup 70 which received 1.25 cc. of blood in the cisterna magna and died sixty-two days later.



Fig. 2.—A section taken from the base of an adult dog which received four injections of blood from 1 to 1.5 cc. in amount into the cisterna magna over a period of seventeen days. The animal was killed two days after the last injection. The meninges were thickened and the seat of active cell proliferation.



pup (35, table 4) that had had five injections, three over the cerebral cortex and two at the base over a period of forty-two days. The first injection was given when the dog was 10 days old. When killed sixty-three days after the first and twenty-one days after the last injection, the general condition was fair. All the organs were normal except the brain. The dilatation of the ventricles was definite when compared with that of the control pup. Examination of the meninges showed chronic thickening over the base and cortex similar to that shown in figure 11. Another striking example was seen in a pup (54, table 1) which when 3 months old weighed scarcely half as much as the control. This pup had general convulsive seizures almost two months after the

TABLE 1.—*Protocols of Pups in Which Convulsions Occurred*

Date	Amount Injected	Remarks	Lesions
<b>Pup 46</b>			
April 23, 1926	1 cc. in cisterna magna	Satisfactory recovery	Meningeal thickening more marked over cerebral cortex where there is some scarring
June 7	.....	Severe general convulsions	
June 9	.....	Died	
<b>Pup 50</b>			
April 26, 1926	1 cc. in ventricle	Recovery	Meningeal thickening over cortex, chiefly at sulci; none over base
May 14	3.5 cc. over left cortex	Recovery	
May 17	2.5 cc. over right cortex	Recovery	
June 9	.....	Severe convulsive seizures; died	
<b>Pup 54</b>			
Jan. 21, 1927	0.5 cc. in cisterna magna	Respiratory embarrassment	Meningeal thickening at base and some areas of the cortex with cortical scarring
Feb. 11	0.8 cc. in cisterna magna	Very limp for some minutes following injection	
May 2	.....	Severe general convulsive seizures	
July 13	.....	Series of general convulsive seizures; died	
<b>Pup 56</b>			
Feb. 2, 1927	0.5 cc. in cisterna magna	Rapid recovery	Brain not sectioned; in poor condition when received in the laboratory
Feb. 4	1 cc. in cisterna magna	Rapid recovery	
May 18	.....	General convulsive seizure	
May 19	.....	General convulsive seizure	
Aug. 15	.....	Died	

last injection. Scattered areas of meningeal thickening were found during the examination of the brain, and there were areas of cortical scarring associated with the thickening (fig. 13).

Convulsive seizures immediately followed the injection in five of the ten adult dogs in which the blood was injected over the cerebral cortex, and in one of the four dogs in which blood was injected into the lateral ventricles. Convulsions did not occur immediately following the injections when young pups were used.

Four of the twenty-six puppies that received injections had convulsions after complete recovery from the immediate effects of the injection without indication of the seizure until a few minutes before the attack. The first pup (46, table 1) had a convulsion twenty-three days after the last injection; he survived for thirty-six hours, during which time there were a great many seizures. The second pup (50,

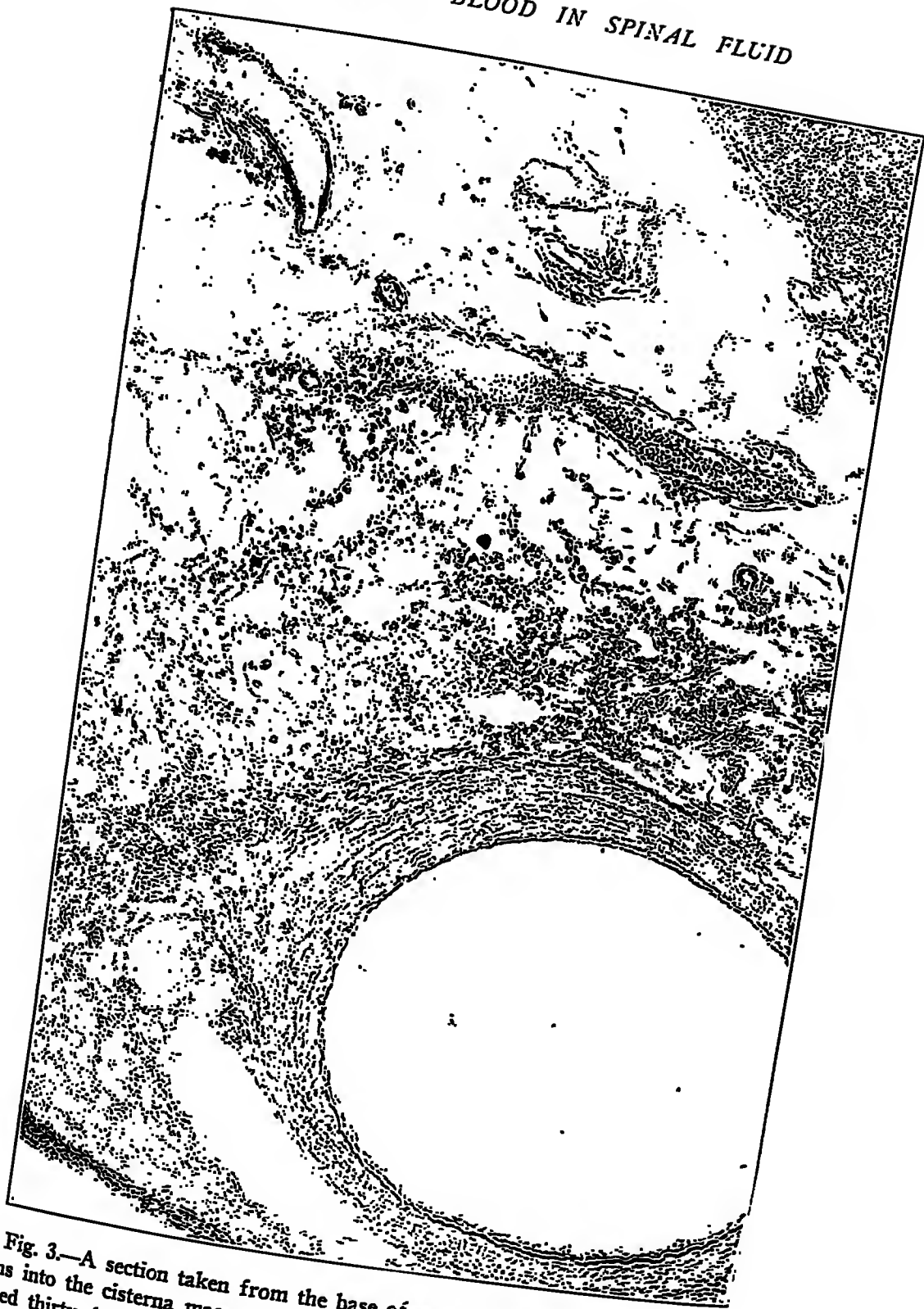


Fig. 3.—A section taken from the base of an adult dog which had four injections into the cisterna magna over a period of thirty-one days; the animal was killed thirty days after the last injection. In comparison with figure 2 there is a diminution of cells, but an increase of fibrous tissue. The fibrous tissue contains a number of pigment-loaded phagocytes.

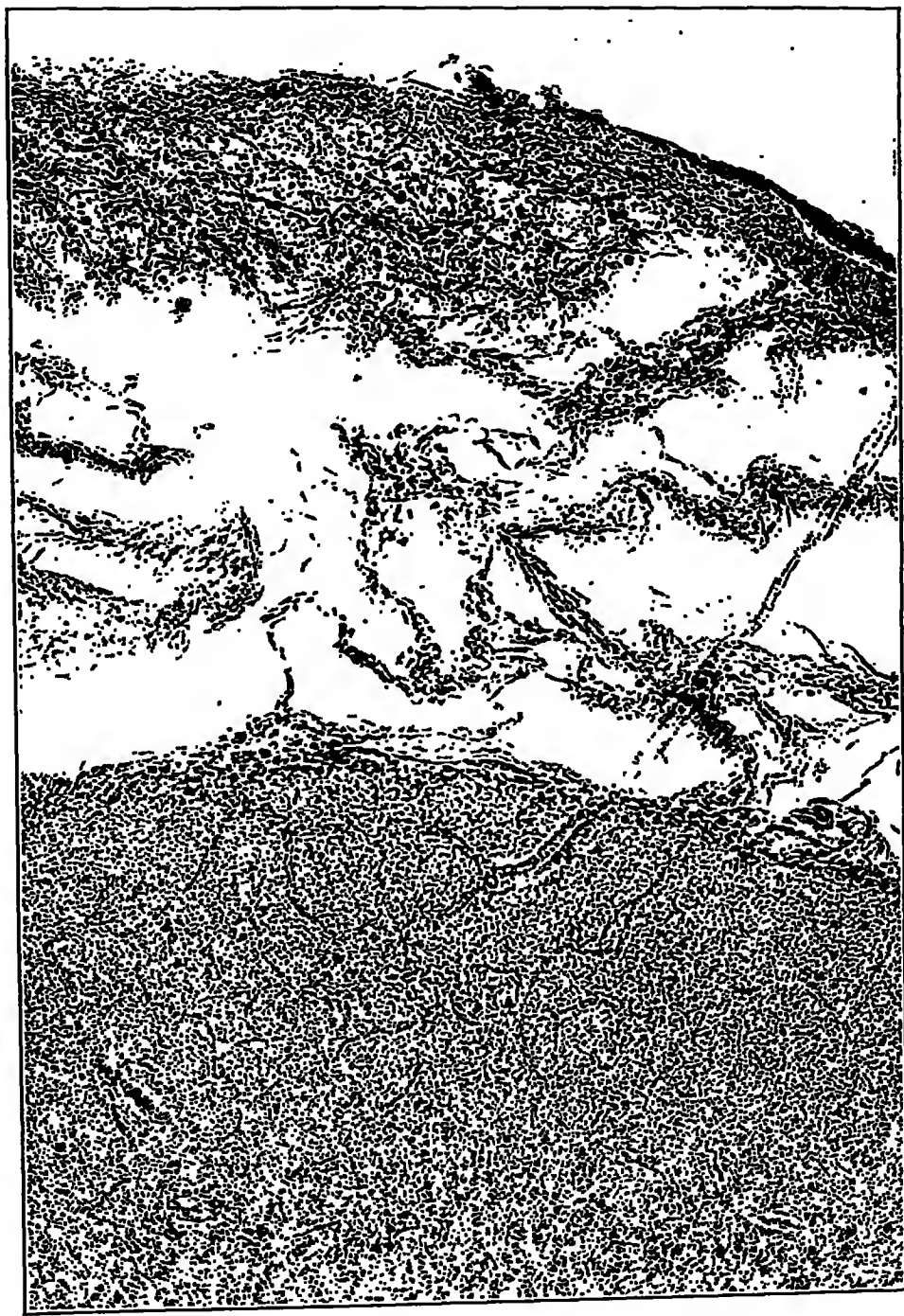


Fig. 4.—A section taken from the crest of a gyrus adjacent to the longitudinal sinus of the same dog as figure 3 showing an increase of fibrous tissue elements.

table 1) had its first convulsion forty-five days after the last injection; this seizure was followed by many others and he died during the same day. In the third pup (54, table 1), the first seizure occurred eighty days after the last injection; from this it recovered promptly and remained fairly well for seventy-two days when, without warning, there was a second series of convulsions in which the animal died. The fourth pup (56, table 1) had single convulsions ninety-three and ninety-four days after the last injection; it recovered from these. It was kept under observation eighty-seven days, during which time it did not have convulsions; but it was aggressive and ill-tempered, and was killed in a fight with another dog.

The seizures were all similar, starting with fine twitchings of a muscle group, usually the face and then spreading over the entire body.

TABLE 2.—*Protocols of the Pups with General Musclic Twitching*

Date	Amount Injected	Remarks	Lesions
<b>Pup 59</b>			
Feb. 28, 1927	0.8 cc. in cisterna magna	Satisfactory recovery	Moderate meningeal thickening at base
March 9	0.5 cc. in cisterna magna	Recovery	
March 28	1 cc. in cisterna magna	Recovery	
May 6	.....	Weak and sick in appearance; twitching	
May 8	.....	Weak with irregular twitching of all muscles, rhythmical twitching of the right hind leg; head drawn to right	
May 9	.....	Irregular twitching of all muscles, rhythmical twitching of right foreleg; died	
<b>Pup 61</b>			
Feb. 28, 1927	1.5 cc. in cisterna magna	.....	Very slight meningeal thickening at base
March 28	.....	Very poor condition; twitching, unsteady, restless and listless	
March 29	.....	Died	

The animal would soon lose consciousness and fall. The facial expression before loss of consciousness showed marked anxiety. Following the attack, the animal was dull and stupid and remained so between the seizures when they occurred in series.

In addition to the four pups which developed convulsions, two were observed forty-three and twenty-nine days, respectively, after the last injection, with severe twitchings involving all the muscles of the body without loss of consciousness. In one of these, pup 61 (table 2), the twitchings continued throughout the day; the dog was greatly weakened and died during the night. Another, pup 59 (table 2), previously well, had twitchings for three days, and on the morning of the third day was weak and twitched constantly; he died before noon. On the lateral surface of the tongue, there was a laceration which was perhaps due to biting during a general convulsive seizure in the night.



Fig. 5.—A section from the mesial wall of the hemisphere adjacent to the falx showing meningeal thickening at the top of a sulcus. The dark cells are phagocytes filled with blood pigment. At *A* two pigment filled phagocytes are seen in the perivascular space.



Fig. 6.—A section taken from dog 10 showing the matting together of the meninges, which is the forerunner of cortical alterations.

Convulsions or muscle twitchings were not observed in six other pups (table 3) which died from nine to sixty-three days after the injections.

In addition to the foregoing twelve puppies that died as the result of the injection, eight pups that had received injections and two controls were killed for histologic study when about half grown. Six of the pups that received injections are living and apparently well. More than one year had elapsed since the last injection was made into the six living puppies. At this time these animals do not show any ill effects resulting from the injection. They will be killed for histologic

TABLE 3.—*Protocols of the Pups Which Died Without Having Had Convulsions or Muscle Twitchings*

Date	Amount Injected	Remarks	Lesions
Pup 32			
March 26, 1926	3 cc. over right cortex	Satisfactory recovery	Meningeal thickening
April 4	.....	Died	over cortex
Pup 33			
March 12, 1926	1 cc. over right cortex	Satisfactory recovery	Moderate degree of
March 26	2.5 cc. over right cortex	Satisfactory recovery	meningeal thickening
April 4	.....	Died	over the right and left cortex
Pup 34			
March 12, 1926	1 cc. over right cortex	Satisfactory recovery	
March 23	3 cc. over right cortex	Satisfactory recovery	Meningeal thickening
April 16	4 cc. over right cortex	Satisfactory recovery	over cortex with some
April 20	3 cc. over right cortex	Satisfactory recovery	scarring
April 28	2 cc. over right cortex	Satisfactory recovery	
May 13	.....	Died	
Pup 36			
March 19, 1923	3 cc. over right cortex	Satisfactory recovery	No section; brain in
March 29	3 cc. over right cortex	Satisfactory recovery	poor condition when
April 16	4 cc. over right cortex	Satisfactory recovery	received in the lab-
April 20	3 cc. over right cortex	Satisfactory recovery	oratory
April 28	2.5 cc. over right cortex	Slow recovery	
May 17	.....	Died	
Pup 44			
April 23, 1926	1 cc. in cisterna magna	Satisfactory recovery	No section; brain in
June 9	.....	Died	poor condition when
			received in the lab-
			oratory
Pup 70			
March 28, 1927	1.25 cc. in cisterna magna	Satisfactory recovery	Moderate degree of
May 30	.....	Died	meningeal thickening
			at base

purposes when full grown. Of the five controls, two that were killed for histologic study seemed entirely normal at the time they were killed, and the three remaining control dogs are living and well.

#### LESIONS

The study of the brains of the animals that died a short time after the last injection showed grossly blood staining of the portion of the meninges with which blood had come in contact and thickening of the stained membrane. In the brains removed long after the last injection, the gross appearance varied from slight thickening of the meninges to normal. Frontal sections through the ventricles of the forebrain showed a degree of dilatation of the ventricles varying from slight to well





Fig. 7.—A section of cortex adjacent to a sulcus in which there is matting of the meninges. Active cell proliferation within the cortex is shown.





Fig. 8.—A further stage of cortical scarring following the cell proliferation as shown in figure 7.

marked. In the adult dogs, ventricular dilatation was less frequent than in the case of the pups. Of the seven adult dogs given one or more injections over the cortex and of the seven adult dogs given one or more injections into the cisterna magna, only one dog (10, table 4) showed a well marked dilatation of the ventricles (figs. 1-3). This animal was given six injections of blood into the cisterna magna over a period of thirty-nine days and was killed two days after the last injection.

TABLE 4.—*Protocols of Animals with Dilatation of the Ventricles*

Date	Amount Injected	Remarks	Lesions
<b>Dog 10</b>			
Jan. 23, 1925	1 cc. in cisterna magna	Satisfactory recovery	Marked meningeal thickening of meninges, at base and in some areas of cortex
Feb. 4	1.5 cc. in cisterna magna	General convulsion	
Feb. 9	1.5 cc. in cisterna magna	Slow recovery	
Feb. 18	1.5 cc. in cisterna magna	Satisfactory recovery	
March 1	2 cc. in cisterna magna	Slow recovery	
March 8	1 cc. in cisterna magna	Slow recovery	
March 5	.....	Killed	
<b>Pup 31</b>			
March 12, 1926	1.5 cc. over right cortex	Satisfactory recovery	Marked meningeal thickening over base and cortex
March 29	2.5 cc. over right cortex	Satisfactory recovery	
April 12	2 cc. in cisterna magna	Satisfactory recovery	
April 20	.....	Killed	
<b>Pup 35</b>			
March 17, 1926	3 cc. over right cortex	Satisfactory recovery	Moderate meningeal thickening at base, not much over cortex
March 24	0.5 cc. over right cortex	Slow recovery	
March 29	2.5 cc. over right cortex	Satisfactory recovery	
April 16	1 cc. in cisterna magna	Satisfactory recovery	
April 28	2.5 cc. in cisterna magna	Satisfactory recovery	
May 10	.....	Killed	
<b>Pup 37</b>			
March 17, 1926	3 cc. over right cortex	Satisfactory recovery	Marked meningeal thickening at base and moderate over cortex, especially at sulci
March 26	3 cc. over right cortex	Satisfactory recovery	
April 12	1 cc. in cisterna magna	Satisfactory recovery	
April 28	1.5 cc. in cisterna magna	Satisfactory recovery	
May 5	.....	Killed	
<b>Pup 45</b>			
April 23, 1926	2 cc. in cisterna magna	Satisfactory recovery	Very slight meningeal reaction over base
May 14	.....	Killed	
<b>Pup 47</b>			
April 23, 1926	1 cc. in cisterna magna	Satisfactory recovery	Moderate degree of meningeal thickening at base
April 30	2 cc. in cisterna magna	Satisfactory recovery	
May 10	.....	Killed	
<b>Pup 70</b>			
March 23, 1927	1.25 cc. in cisterna magna	Satisfactory recovery	Moderate degree of meningeal thickening at base
March 29	.....	Died	

Six of the nineteen puppies which had received injections and on which autopsies have been performed had definite dilatation of the ventricles (fig. 1). As shown by the protocols, all of the puppies with dilated ventricles had been given one or more injections into the cisterna magna; in addition, in some injections were given over the cortex. Two of the pups (45 and 70, table 4) received only one injection, one 2 cc. and the other 1.25 cc. of blood into the cisterna magna. One of the pups was killed twenty-one days after the last injection. The dilatation of the ventricles was always associated with meningeal thickening. Clinically, the animals did not show any evidence of the dilatation.



Fig. 9.—Active cell proliferation in the meninges covering the optic nerve. The section was taken from dog 10.



Fig. 10.—A section taken from the optic nerve of one of the control mice showing the normal meningeal coverings of the nerve.



Fig. 11.—A section from the base of the brain of pup 46 which died following convulsive seizures forty-seven days after an injection of 1 cc. of blood in the cisterna magna. There is marked meningeal thickening with cell infiltration.

The microscopic study of the brains showed meningeal thickening where blood came in contact with the membranes. In the acute stage, that is in the dogs killed soon after the last injection, the meninges showed marked cell proliferation. In figure 2, the thickened membrane is shown at the base of the brain of a dog that had been given four injections into the cisterna magna over a period of seventeen days and was killed two days after the last injection. The chronic stage of this condition is shown in figure 3, a photomicrograph from the base of the brain of an animal killed thirty-three days after the last injection. During the thirty-three days, the clinical condition was not satisfactory in that the animal ate poorly and was very weak.

This condition is not limited to the base of the brain as shown in figure 4, which is an illustration of a section taken from the same dog over the crest of the gyrus adjacent to the longitudinal sinus. The meningeal thickening is often marked at the site of sulci diminishing as the crest of the sulcus is reached. In figure 5, taken from dog 10 (table 4), the meningeal thickening at a sulcus is seen. The heavily stained cells are phagocytes filled with blood pigment. The pigment-laden cells are found even in the chronic state of the meningeal thickening secondary to the injection of blood and are useful in the microscopic examination of the specimens, as is blood-staining in the gross appearance in determining the areas of the meninges with which the blood had come in contact.

In figure 5, at *A* two pigment filled phagocytes are seen in a perivascular space well below the surface of the cortex, indicating an early stage of cortical alteration. This cortical alteration is frequently secondary to a condition seen in figure 6, where it is shown that the meningeal reaction has progressed to a point of matting together of the membranes in a sulcus, entirely obliterating the normal meningeal spaces. With a beginning cortical alteration, as seen in figure 5, active cell proliferation (fig. 7) ensues, which progresses for a time and results in fibrous tissue deposit constituting a scar, as shown in figure 8.

The meningeal reaction extends to the membranes covering the optic nerve, as shown in figure 9, a photograph of a section of the optic nerve and its coverings taken from dog 10 as compared with the same structures in figure 10, taken from one of the control puppies.

In the pups that presented symptoms and in those that died, meningeal thickening as shown in the previous sections was observed. For example, in figure 11, taken from the base of the brain of pup 46 (table 1), the meninges are thickened and contain a large amount of fibrous tissue. A photograph (fig. 13) taken from the occipital pole of the brain of pup 54 shows the meninges of a sulcus in active cell proliferation extending into the cortex at the site of a blood vessel.



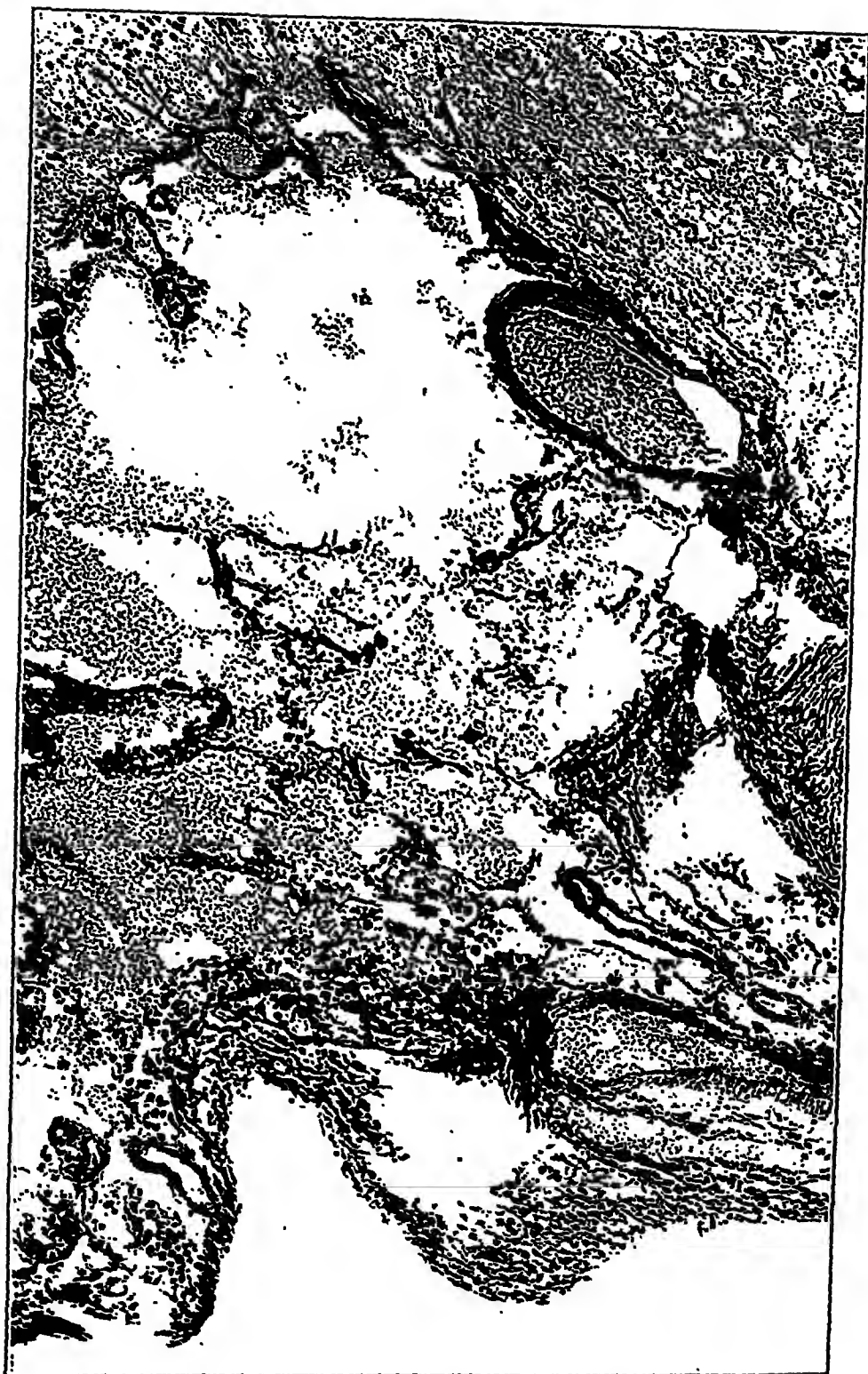


Fig. 12.—A section of the meninges from the base of pup 59 which died during convulsions forty-two days after receiving three injections of blood into the cisterna magna showing an increase of fibrous tissue elements.



Fig. 13.—A section taken from the occipital pole of prep 54-6, with evidence of thickening in a sulcus with beginning cortical alteration.



## CONCLUSIONS

Blood mixed with the cerebrospinal fluid of young and adult dogs produces neurologic disturbance varying from slight difference in behavior to severe convulsive seizures. Though some of the animals were severely affected by small quantities of blood mixed with the cerebrospinal fluid, others have survived more than a year, and are apparently normal.

Following the introduction of blood into the cerebrospinal fluid, there begins a reaction of the parts of the meninges which have come in contact with the blood. The meningeal reaction tends to subside and may disappear as the blood disappears from the fluid. After several weeks, the cell elements are less numerous in the meninges, but a large amount of fibrous tissue is present.

Late in the course of the meningeal reaction, changes in the structure of the cortex are observed.

Moderate dilatation of the ventricle not infrequently occurs following the introduction of blood into the cerebrospinal fluid of young pups. The condition may occur in adult dogs, but with less frequency.

These facts as applied to patients with bloody cerebrospinal fluid are discussed in part B of this paper.

This work has been carried on under the direction of Dr. Adolf Meyer. Dr. Frank Ford assisted in some of the experiments and Miss Cecelia Bisson in the making of the motion picture films, for the study of the behavior of the animals, and in making the illustrations for this paper.

# BLOOD IN THE CEREBROSPINAL FLUID

## RESULTANT FUNCTIONAL AND ORGANIC ALTERATIONS IN THE CENTRAL NERVOUS SYSTEM \*

### B. CLINICAL DATA

CHARLES BAGLEY, JR., M.D.

BALTIMORE

In a report concerning some experiments made to determine the effect of a relatively small amount of blood in the cerebrospinal fluid,<sup>1</sup> attention was directed to the acute and chronic symptoms resulting from the meningeal irritation caused by the blood. The present report concerns some experiences with bloody cerebrospinal fluid in patients ranging in age from a few days to 56 years who presented meningeal lesions similar to those produced in the experiments.

The sudden appearance of blood in the cerebrospinal fluid of the very young or of middle-aged persons is rare enough to excite one's curiosity as to the cause of the bleeding. The first part of this paper deals with the examination of the brains in some of the fatal cases and the lesions responsible for the blood.

### REPORT OF CASES

*CASE 1.—Venous plexus of cerebellar pia; drainage of cerebrospinal fluid without benefit.*

Baby G. was admitted to the hospital when 16 days old. Labor was uncomplicated, and the child seemed normal in every way until 15 days old, when the mother noticed twitchings of the muscles of the body, drawing back of the head and rolling of the eyes. The following day there were several severe convulsions. Lumbar puncture, performed when the patient was admitted to the hospital, showed bloody cerebrospinal fluid. The drainage of this fluid did not improve the condition, and on the following day an opening was made in the right temporal region. When the dura was incised, there was little cerebrospinal fluid in the subarachnoid space, the cortical veins were dilated, and old blood was seen. The absence of cerebrospinal fluid was in striking contrast to the condition usually found in simple hemorrhages at birth. Drains were inserted beneath the dura. Following the operation there was not the usual free drainage of cerebrospinal fluid, and several lumbar punctures were made. In all of these punctures the fluid was bloody, and eighteen days after the operation it was concluded that a large blood clot was present. As there was no indication of the location of the supposed clot, further exploration was not attempted. treatment and

abandoned, and the child died fifty-one days after birth. Autopsy revealed a venous plexus covering the greater portion of the cerebellar cortex (fig. 1) and marked dilatation of the ventricle as shown in figure 2.

On section, the pia was seen to be much thickened and contained a great many dilated, thin-walled veins, as shown in figure 3. The sudden appearance of symptoms was due to rupture of a vein. Repeated punctures failed to clear the fluid because of recurrent bleeding from this source. The dilatation of the ventricles was due to the adhesions at the foramina of Magendie and Luschka. Hydrocephalus secondary to hemorrhage in the posterior fossa has been described by Arthur G. Jacobs<sup>2</sup> in the case of a new-born child with early evidence of hemorrhage. Seventy-five days after birth, suboccipital exploration by Dr. R. E. Semmes revealed extensive adhesions and arrested the condition.



Fig. 1 (case 1).—Greater part of the cerebellum is covered by a network of veins. Rupture of one of these veins was the cause of the hemorrhage fifteen days after birth.

*CASE 2.—Venous plexus involving chiefly the occipital and cerebellar veins; extravasation of a small amount of blood from a cerebellar vein with signs of increased intracranial tension.*

M. H., a girl, aged 20, had a history of normal development until the age of 6 years, when she had had a severe attack of measles, since which time she had not been strong. At the age of 12, she was extremely ill with influenza, and at that time a heart murmur with cardiac enlargement was found. At the age of 16, a murmur was first heard in the head. During the four years preceding the examination, headache was troublesome; it became severe after an attack

2. Jacobs, A. G.: Hydrocephalus Following Intracranial Hemorrhage, South. M. J. 19:669 (Sept.) 1926.



Fig. 2 (case 1).—The frontal section of the brain showing marked dilatation of the ventricles secondary to hemorrhage in the posterior fossa.



Fig. 3 (case 1).—Showing one of the many dilated blood vessels in the cerebellar cortex.

of otitis media twelve weeks before the examination, at which time a mild degree of choked disk was noted. These facts suggested the possibility of an abscess of the brain. Two weeks before the examination, while stooping to fasten her galoshes, she was suddenly aware of a brushing sound, which she thought was caused by some one passing her in the room. This was immediately followed by a severe headache, vomiting and dizziness. Lumbar puncture ten days later showed marked increase in pressure and evidence of a small amount of old blood in the cerebrospinal fluid. When examined four days after this puncture, the patient was stuporous but could be aroused. The examination revealed a loud systolic murmur over the precordium extending into the neck and a loud bruit over the entire head synchronous with the heart beat. There

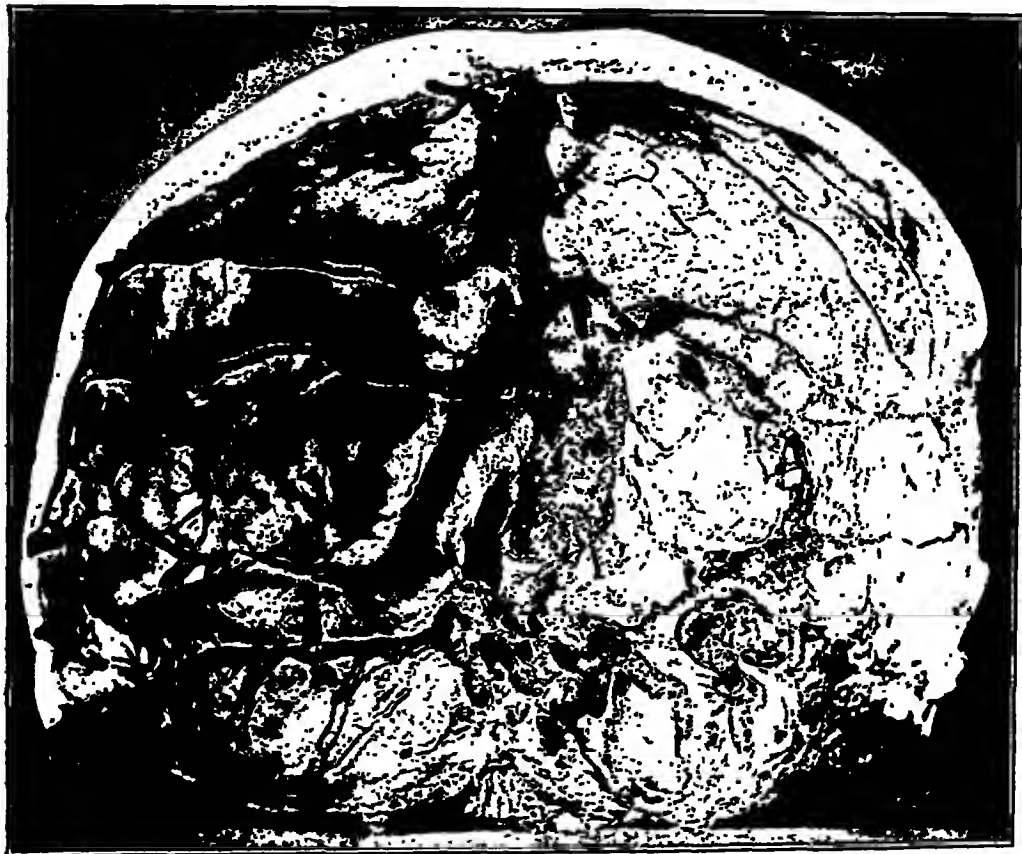


Fig. 4 (case 2).—The posterior part of the skull including the occipital and part of the parietal bones, showing the deep depressions corresponding to the greatly dilated venous sinuses and tributaries.

was marked spontaneous nystagmus and a high degree of choked disk. The diagnosis of a cerebral vascular lesion, exact type unknown, with leakage of blood into the cerebrospinal fluid was made. Because of the likelihood of exciting further bleeding, a lumbar puncture or a more radical operative procedure was not undertaken. Two weeks later, the patient was in a serious condition because of increased intracranial pressure, and she died twenty-four hours after an attempt at relief through a right subtemporal decompression.

Postmortem examination showed that the lesion involved chiefly the venous structure of the dura, resulting in deep channeling of the skull as shown in figure 4. In the left cerebellar pontile angle, several dilated and recently

thrombosed veins were seen (fig. 5). Sections of the area of extravasation showed several thin-walled veins (fig. 6). A large clot was not found; the marked increase in intracranial pressure was evidently due to the irritation of the bloody cerebrospinal fluid. Leakage had, no doubt, been occurring over a period of fifteen weeks, corresponding to the course of the final illness.

**CASE 3.**—*Recurrent hemorrhage following rupture of an aneurysm of the anterior cerebral artery, with signs of increased intracranial tension.*

E. S., a girl, aged 12, entered the hospital with a history of a sudden severe headache thirty-five days before admission. The headache was associated with vomiting. A week later, because of continuance of symptoms, she was admitted to the Western Maryland Hospital in Cumberland, and lumbar puncture at that time revealed bloody cerebrospinal fluid. Twelve days later, she was discharged from the hospital with marked improvement in symptoms, though she was rather dull and vision was blurred. Thirty-one days after the first attack of headache, she had a second severe attack with two general convulsive seizures, diplopia and



Fig. 5 (case 2).—Marked venous dilatation with recent thrombus in the cerebellar pontile angle.

badly blurred vision. Five days later, she was admitted to the Church Home and Infirmary, Baltimore, where I first saw her. At the time of admission, there was severe headache, vomiting and stupor (though she could be aroused) and a very high grade choked disk, with hemorrhages; the right pupil was larger than the left, and a loud cerebral bruit was heard over the entire head, but more distinctly in the temporal regions. When questioned, the child said that she had heard the murmur for a long time. Bloody cerebrospinal fluid was obtained on lumbar puncture. A right subtemporal decompression for relief of pressure was made, and the child died four days after operation. Figure 7 shows a large hemorrhage between the hemisphere extending into the left lateral ventricle. Microscopic study of this area showed an organized blood clot, the result, no doubt, of the bleeding which caused the original attack thirty-five days before admission to the hospital, a large amount of recent hemorrhage and an aneurysmal dilatation of the right anterior cerebral artery (fig. 8). Rupture of the aneurysm was the cause of the bleeding.

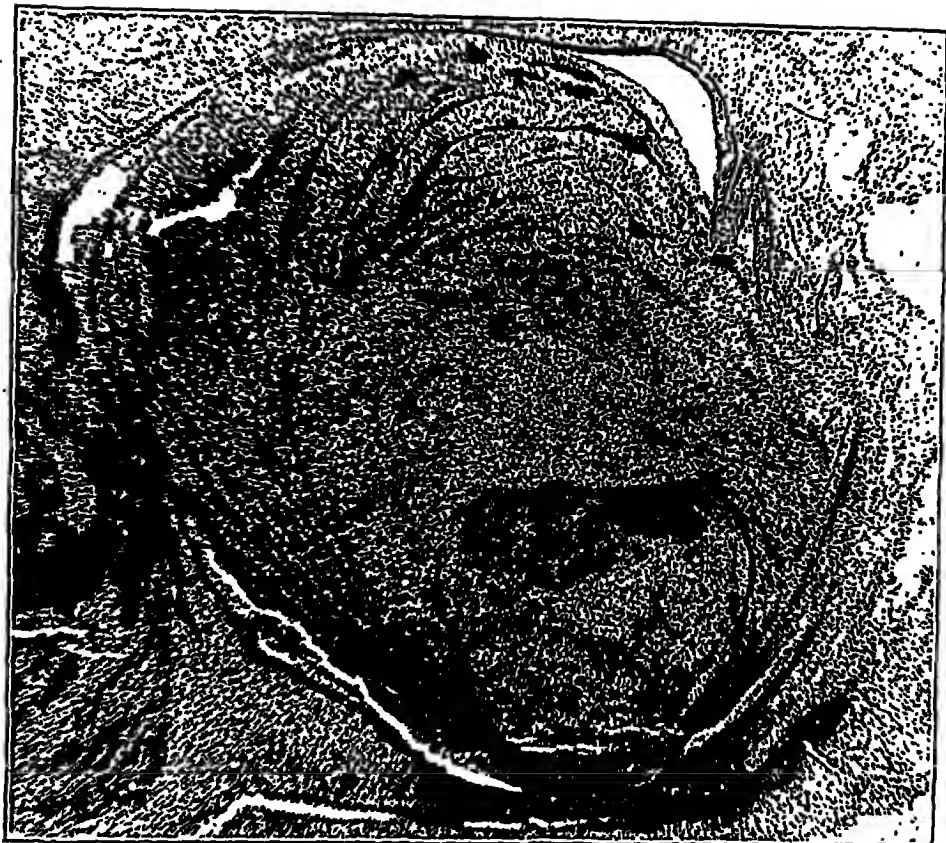


Fig. 6 (case 2).—A higher magnification of the vein in figure 5, showing the breaking down of the thin wall of the vein and recent thrombus.

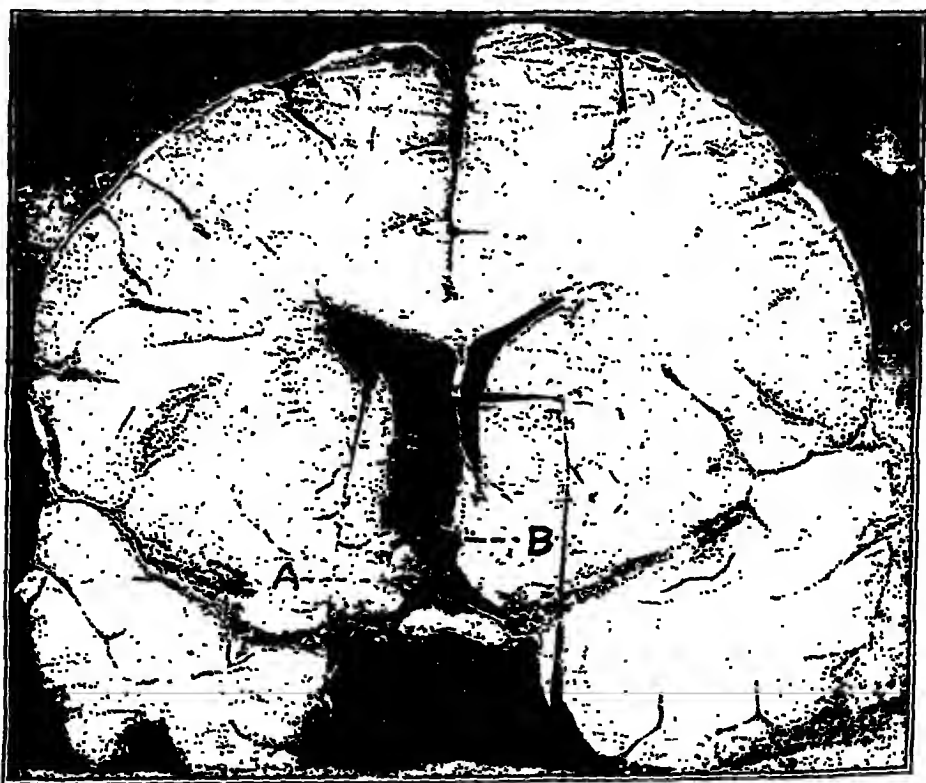


Fig. 7 (case 3).—Between the hemispheres there is a blood clot extending from the base into the left ventricle. At *A*, the cut end of the left anterior cerebral artery is seen; at *B*, an aneurysm of the right anterior cerebral artery.

CASE 4.—Hemorrhage due to rupture of an aneurysm of the anterior cerebral artery. Death followed the initial rupture.

C. B., a man, aged 37, previously in good health, was suddenly seized with severe headache and vomiting, followed almost immediately by coma. He died





section of the brain, as seen in figure 9, showed a bulbous enlargement of the anterior cerebral artery. Sections of this unruptured aneurysm are shown in figures 10 and 11. This lesion was not the source of the hemorrhage; a second small aneurysm of the artery ruptured subcortically. Small aneurysms of this type are frequently multiple.

**CASE 5.**—*Recurrent hemorrhage following rupture of an aneurysm of the anterior cerebral artery.*

M. H., a man, aged 41, was admitted to the hospital complaining of headache and weakness of the left side of the body. The illness began three months before admission with sudden loss of consciousness. Five weeks after the onset the patient again lost consciousness, and there was paralysis of the left side of the body; this gradually improved until the time of admission to the hospital. The

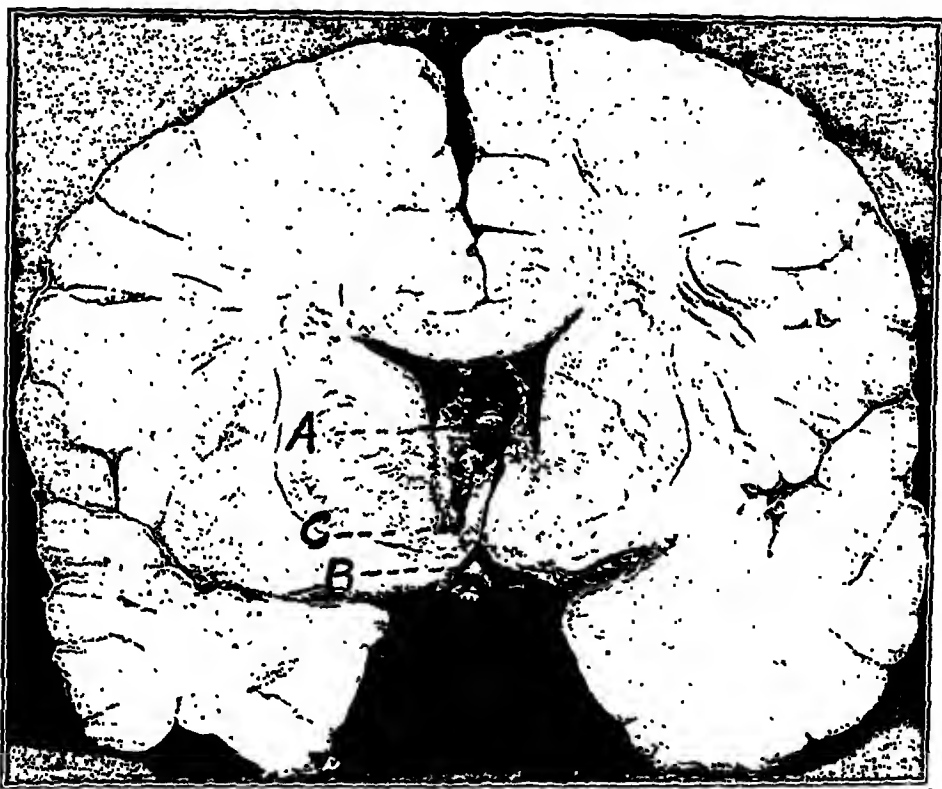


Fig. 9 (case 4).—*A* shows blood clot resulting from the rupture of a branch of the left anterior cerebral artery at *C*. *B* indicates aneurysm of the anterior cerebral artery unruptured, shown in figure 10.

examination showed partial hemiplegia of the left side and arteriosclerosis. The Wassermann test of the blood and spinal fluid was negative, and the spinal fluid contained 13 cells. Four days after admission to the hospital, the patient suddenly lost consciousness, but he improved during the following hour, at which time there was complete loss of power of all muscles of the left side of the body. He again lost consciousness and died two hours after the onset of the attack. The history did not mention a cerebral bruit, so that it is not possible to say whether or not one was present. Autopsy showed general arteriosclerosis, free blood over the right cerebral cortex and a partially organized blood clot at the base between the hemispheres of the brain anterior to the chiasm, as shown in figure 12.

Section of the blood clot showed an aneurysm of the right cerebral artery as shown in figure 13.

**CASE 6.**—*Recurrent hemorrhage in a patient at the age of 22, 42 and 44 years; large calcified mass at the site of the first hemorrhage and beginning calcification in the second with an aneurysm of the anterior cerebral artery; death two hours after the third hemorrhage.*





Fig 11 (case 4).—Higher magnification ( $\times 125$ ) of *A* in figure 10, showing the abrupt termination of the elastic tissue.

was a mild degree of choking of both optic nerves. The roentgenogram showed a smooth, calcified mass 1 cm. above and not connected with the sella turcica (fig. 14). In the anteroposterior view, this mass was seen exactly in the midline (fig. 15). The patient said that at the age of 22 he had had a similar illness which had necessitated his remaining in bed for six weeks, but he had entirely recovered. This fact led to the opinion that the calcified mass shown in the roentgenogram had to do with the previous illness. The smooth external surface of the mass suggested calcification in a cyst, and tumor calcification was ruled out. Soon after the patient's admission, the symptoms improved, and he was discharged from the hospital on the twenty-second day. In spite of the fact that a bruit was not heard and a lumbar puncture could not be made because of the danger of exciting further bleeding, it was concluded that the patient had a vascular lesion and that the attacks were due to bleeding as had been found in

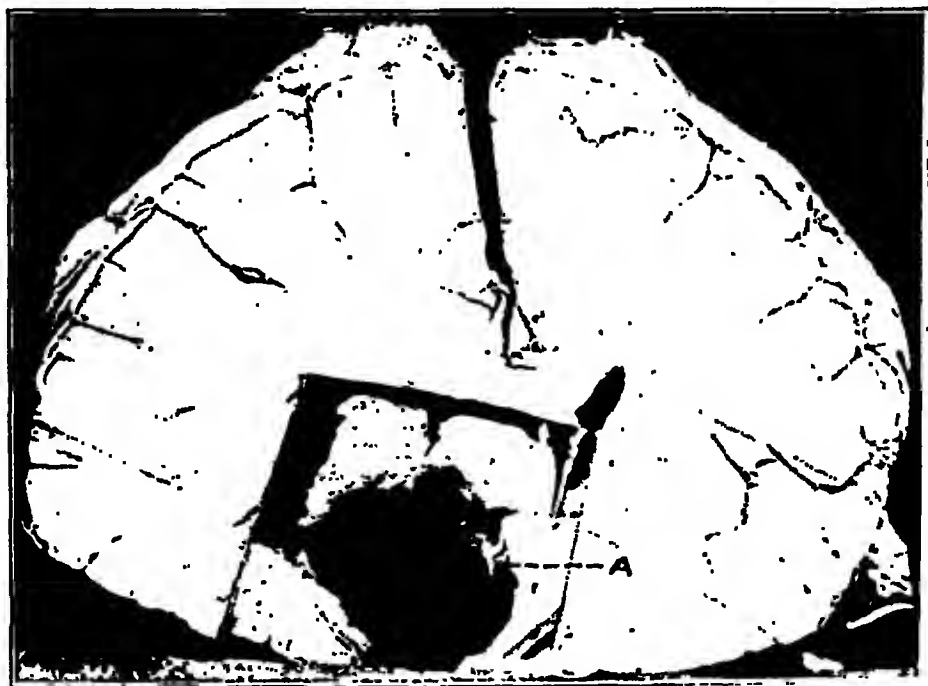


Fig. 12 (case 5).—Blood clot between the frontal lobes with the left anterior cerebral artery at *A*.



Fig. 13 (case 5).—Section taken from the area of blood clot in figure 12, showing the left anterior cerebral artery at *A* and the right anterior cerebral artery with an aneurysmal dilatation. The termination of the elastic tissue marking the extent of the arterial wall is shown at *B* and *C* below which the aneurysm extends.



Fig. 14 (case 6).—Above the sella turcica a calcified mass is seen.

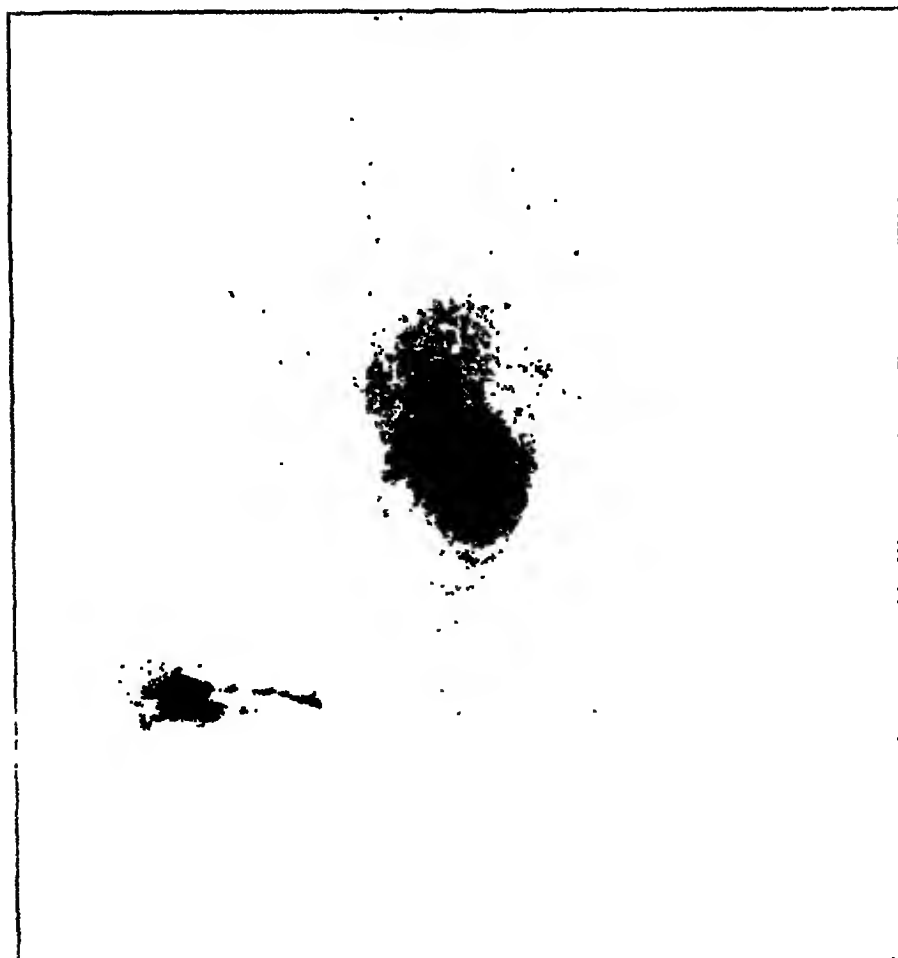




Fig. 16 (case 6).—Frontal section showing dilatated ventricles which were filled with fresh blood and the calcified mass at *A* shown in figures 14 and 15.



Fig. 17 (case 6).—Anterior cerebral aneurysm at *A* and calcified cyst at *B*.

death. In the wall of this mass beginning calcification was seen, and it is probable that this would have been similar to the large calcified mass if the patient had survived. In figure 18, the anterior cerebral artery at the caudal extremity of the aneurysm is shown. The thick wall of the aneurysm in this



Fig. 18 (case 6).—Anterior cerebral artery at its junction with the aneurysm shown at A in figure 17. The elastic tissue present from B to C is absent between the points of the arrows.

section was lacking in elastic tissue. Sections through the large sac as shown in figure 17 also demonstrated complete absence of elastic tissue.

CASE 7.—Clinical evidence of hemorrhage in the same area as shown in the three preceding cases in which the patients recovered following the initial attack.



Mrs. R. R., a woman, aged 34 years, while walking with her husband in the garden, suddenly exclaimed, "I have the funniest feeling in my head and it hurts. I am going into the house and lie down." I saw this patient three days later, when stupor, nausea and vomiting, marked bilateral edema of the disks with hemorrhages and abducens weakness were present. The cerebrospinal fluid, as obtained by lumbar puncture, was slightly bloody. Only a small amount of fluid was taken, and the puncture was not repeated because of the presence of choked disk and the possibility of exciting further bleeding. A cerebral bruit was not heard. The symptoms progressed for two days, when there was paralysis involving chiefly the muscles of the right side of the body. The paralysis and choking slowly disappeared, but there was some headache for two months. It is now eight months since the onset of the illness, and the patient is free from symptoms; however, there is grave danger of recurrence of the symptoms.

Until recent years, cerebral aneurysms have been mainly of pathologic interest. Five years ago, Dr. C. P. Symonds and Dr. Harvey Cushing<sup>3</sup> called attention to the importance of clinical facts concerning these lesions. Slight hemorrhage with definite clinical manifestations usually precedes the large fatal hemorrhage in small cerebral aneurysms and must be considered in the differential diagnosis of obscure lesions of the brain.

The source of bleeding in infants is a matter of great importance. The bleeding is frequently due to tearing of the large dural sinuses, but in some cases it is probably due to tearing of the cortical veins as they enter the dura. The following case is included because of its course which typifies what happens when blood escapes into the cerebrospinal fluid and because of the specimen which shows the source of the blood.

**CASE 8.**—*Small amount of blood in the cerebrospinal fluid following cerebral trauma; death in status epilepticus on the third day.*

J. D., aged 6 months, was in excellent physical condition when left with a colored nurse. When the mother returned two hours later, the child was unconscious and the nurse did not give any indication of the cause. Twenty-four hours later the fontanel was tight, and there was a severe general convulsive seizure. Seizures occurred at short intervals until collapse eighty hours after the onset when the child died. Lumbar puncture during the third day revealed bloody cerebrospinal fluid.

Autopsy showed a moderate amount of blood mixed with the cerebrospinal fluid and a small blood clot over the left frontal cortex where a vein had been torn from the dura (fig. 19). The pia-arachnoid was thickened and the veins markedly dilated.

**CASE 9.**—*Tumor of choroid plexus with hemorrhage into ventricle on the tenth day. The early date of bleeding created confusion with birth hemorrhage.*

H. M., came under observation when 10 days old because of sudden increase in intracranial pressure, with vomiting, respiratory embarrassment and loss of consciousness. When the patient was examined about six hours after the onset

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3. Symonds, C. P.: Clinical Study of Intracranial Aneurysms, Part I, *Guy's Hosp. Rep.* 73:139 (April) 1923. Cushing, H.: Clinical Study of Intracranial Aneurysms, Part II, *ibid.* 73:159 (April) 1923.

of the symptoms, the fontanel was bulging and tense, and the cerebrospinal fluid contained a large amount of blood. The late onset of the symptoms without any indication of a hemorrhage during the first hours after birth and the quantity of fresh blood in the cerebrospinal fluid led to the suspicion of a lesion similar to that shown in case 1. Repeated lumbar punctures showed a gradual decrease in the amount of the blood, but the fluid remained yellow, and normal intracranial



Fig. 19 (case 8).—Specimen from an infant, aged 6 months, showing blood clot at the site of a torn cortical vein at point of attachment to dura. The clot is small and merely marks the point of escape of blood into the cerebrospinal fluid, which produced severe convulsive seizures and death.

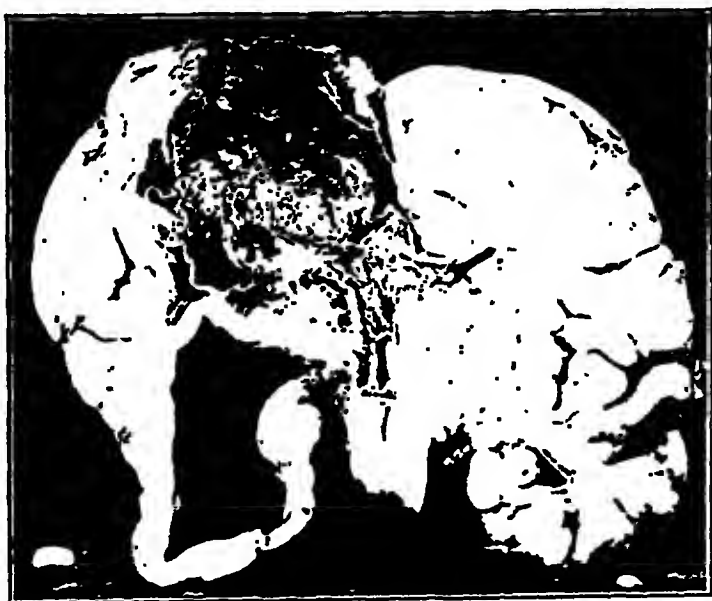


Fig. 20 (case 9).—Tumor of the brain, the source of a large amount of blood in the cerebrospinal fluid on the tenth day after birth.

tension could not be maintained. At the age of 9 weeks the circumference of the head was 40 cm., the fontanel was large and the sutures were separated. With the view to determining the possible presence of hydrocephalus, air was introduced through a lumbar puncture needle. Only the right ventricle was filled

The right ventricle was then aspirated and air was injected, but again only the right ventricle was filled. A left osteoplastic bone flap was removed and a large solid tumor uncovered. The flap was replaced, and the child died twelve days later.

Examination of this tumor, shown in figure 20, proved to be a choroid plexus growth. The foramen of Monro was entirely occluded, and part of the left



Fig. 21 (case 10).—Cerebral meningeal reaction resulting from bloody cerebrospinal fluid due to injury of the spinal cord.

lateral ventricle of the forebrain which was not filled with tumor was greatly distended with blood-stained fluid.

*CASE 10.—Cerebral irritation following bloody cerebrospinal fluid, extracranial source of blood with no likelihood of cranial injury.*

The case of Baby B. is interesting because the injury at birth which was the source of blood was in the spinal cord, the blood reaching the cerebral sub-

arachnoid space in the same manner as in the experiments on dogs when the injections were made into the cisterna magna. The child was born after breech delivery and weighed 9 pounds (4.1 Kg.). From the beginning the condition was not satisfactory, and twelve hours later the temperature was 107 F. The fontanel was bulging slightly, and bloody cerebrospinal fluid was obtained on lumbar puncture. When 36 hours old, the child had two general convulsive seizures and died. The injury of the cord involved the eighth cervical and the first thoracic segments; from this point, blood had reached the cerebral cortex, producing marked clinical disturbance and the first stage of meningeal reaction shown in figure 21.

CASE 11.—*Chronic meningitis in which the clinical course and observations at autopsy suggest early bloody cerebrospinal fluid.*



Fig. 22 (case 11).—Arachnoid mesh at the fissure of Sylvius which before fixation in formaldehyde was greatly distended with cerebrospinal fluid.

M. B., aged 9 months, had had a normal birth and did well until the age of 2 months, when she was irritable and cried a great deal. The feeding was thought to be the cause, but frequent changes in the diet did not improve the condition. Vomiting was troublesome, and there was gradual increasing rigidity. When 6 months old, she had a severe general convulsion, following which the condition grew worse. When admitted to the hospital at the age of 8½ months, the child was undernourished and spastic, it had convulsive movements of the arms and legs, and the head was retracted. The cerebrospinal fluid was clear, with 2 cells per cubic millimeter. When the patient was admitted to the hospital, the temperature was 101.5 F., and it ranged between this and 107 F. until death two weeks later.



Fig. 23 (case 11).—A section from the base of the brain of an infant with clinical evidence of bloody cerebrospinal fluid showing meningeal thickening.

Autopsy revealed chronic meningeal thickening; the arachnoid at the sulci was opaque and edematous; in the sylvian fissure, it had the appearance of a veil-like sponge filled with fluid. In figure 22, the arachnoid mesh in which the fluid was held is shown; fixation of the tissue had caused the membrane to shrink below the level of the surrounding cortex in marked contrast to the distended membrane when seen in the fresh state. The meningeal thickening at the base of the brain is shown in figure 23.

My interest in the subject of bloody cerebrospinal fluid began during the summer of 1923, when the following case came under observation.

*CASE 12.—Chronic meningitis, secondary to birth hemorrhage (clinical evidence). Gradual increase in the head and other indications of hydrocephalus.*

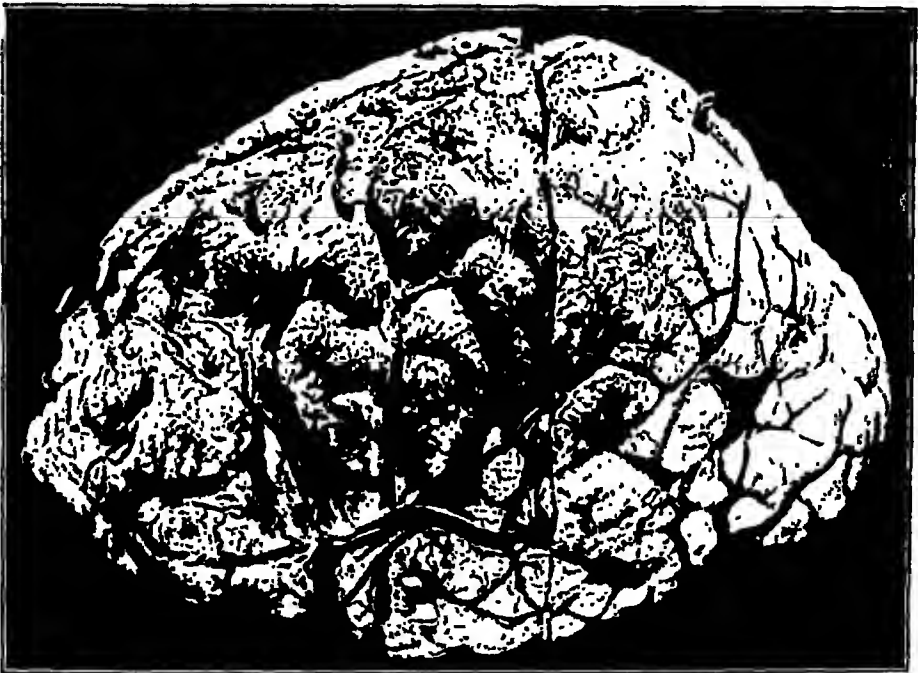


Fig. 24 (case 12).—Chronic meningeal thickening with marked dilatation of the cortical veins.

*Ventricle normal in size, a large amount of fluid over the cerebral cortex. Subtemporal decompression greatly diminished the meningeal thickening on the side drained, but had no influence on the undrained side.*

P. C., aged 27 months, was apparently normal at birth. Jaundice was present on the second day and lasted for some weeks. Vomiting was troublesome on the fifteenth day and had continued irregularly, making it difficult to keep up body nourishment. At the time of the examination, the child weighed 22 pounds (10 Kg.). The appearance of the head indicated hydrocephalus, the fontanel was large, circumference 48 cm., thin, fine hair was present over the scalp, and there was internal squint of both eyes. Air injected into the ventricles showed both ventricles to be of normal size, but a large amount of air escaped over the cortex. A right subtemporal decompression revealed large cortical veins which were matted together, especially in the sylvian fissure. The arachnoid was thickened and

opaque. There was a large amount of cerebrospinal fluid over the cortex. A drain was inserted, and following the operation there was free drainage of cerebrospinal fluid which continued even after removal of the drain. The child died of pneumonia twenty-two days after the operation. The particular interest in this case is found in the examination of the brain, first because of the undilated ventricles in a child with a large head and other indications of hydrocephalus; second, because of the difference in the meninges and meningeal vessels on the drained and undrained sides of the brain. Grossly, the drained side was lighter in color than the undrained side, which was dark and cyanotic, suggesting a venous stasis. The veins of the undrained side were large, and small tributaries were plainly visible (fig. 24), while on the drained side (fig. 25) the veins were smaller, and the tributaries were not seen. Microscopically, the pia-arachnoid was much



Fig. 25 (case 12).—The opposite side of the brain shown in figure 24. When explored twenty-two days before death this hemisphere had the same appearance as that shown in figure 24. Free drainage of cerebrospinal fluid during the interval between operation and death greatly improved the drained side, but seemed to have had no influence on the undrained side.

thickened, the walls of the vessels were heavy and they were dilated on the undrained side. The difference in the membrane at the top of a sulcus is shown in figures 26 and 27. Deep in the sulci, the changes were marked. In figure 28, taken from the undrained side, there is a large amount of fibrous tissue and the vessel walls are thick in sharp contrast to the more delicate arrangement of these structures in figure 29, taken from a sulcus of the drained side. The lesions shown in the examination of the meninges of this brain were like those found in the young dogs following the injection of blood in the cerebrospinal fluid, and were similar to those found in verified cases of bloody cerebrospinal fluid in infants which in some instances presented the same clinical picture so that it



seems fair to assume that this child had a hemorrhage, though lumbar puncture was not performed early.

In its most simple form, bloody cerebrospinal fluid is seen in a type of hemorrhage in the new-born. Such cases show a disturbance ranging from twitching to general convulsive seizures during the first few days immediately following delivery. The story of hemorrhage in the



Fig. 26 (case 12).—The dilated vessels and thickened arachnoid mesh on the undrained side.

new-born has been told many times and need not be repeated here, so that only a few cases illustrating types of cases and methods of treatment are included.

*CASE 13.—Small amount of blood in the cerebrospinal fluid during birth, with mild cerebral disturbance; entirely controlled by repeated lumbar punctures.*



Baby J. F. B., a breech delivery, was apparently normal until about 24 hours of age, when he became limp and cyanosed and had attacks of twitching involving the whole body. These twitchings occurred at intervals of from two to three hours. A lumbar puncture was made on the third day, and yellow cerebrospinal fluid was obtained. The following day there was no improvement in the condition, and a second lumbar puncture was performed. The fluid obtained was more



Fig. 27 (case 12).—Pia-arachnoid on the crest of a gyrus near a sulcus, showing the more delicate arachnoid mesh than in figure 26.

deeply tinged than that withdrawn at the first puncture. During the observation, there were constant jerkings of the entire body—more marked in the left arm. After the second puncture, there was marked improvement in the condition, with milder attacks occurring at longer intervals. On the fifth day, lumbar puncture revealed a more deeply stained cerebrospinal fluid. The fluid flowed without any evidence of pressure. Attacks were not noted after the fifth day. Several

punctures were made during the latter period of the stay in the hospital, and the fluid gradually returned to a normal color.

This child is now entirely normal at the age of 27 months.

With a history such as that obtained in this case, lumbar puncture is always recommended. Care must be taken in doing the puncture to avoid trauma, particularly when done in the first forty-eight hours, and for this reason, I practice giving a few drops of chloroform and use a small Luer hypodermic needle. When bloody fluid is obtained, the child

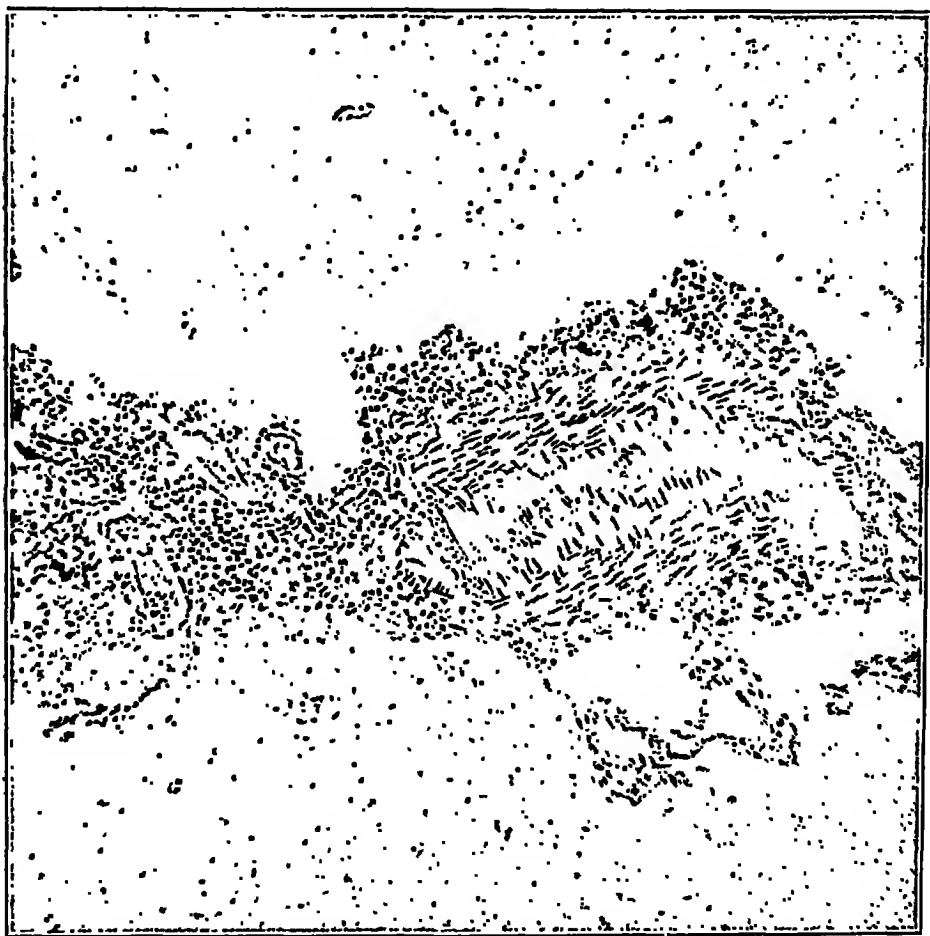


Fig. 28 (case 12).—Pia-arachnoid deep in a sulcus on the undrained side showing fibrous tissue and cell infiltration.

is generally better after the first or second puncture, but I make repeated punctures even in the absence of symptoms until the fluid is entirely clear. The intervals between punctures depend on the severity of the symptoms (being shorter in severe cases) and the amount of blood present. It is recognized that a new-born child with some blood in the cerebrospinal fluid will recover spontaneously, but when the blood has produced symptoms, the normal recuperative powers should be aided by repeated punctures.

Fortunately, the greater number of hemorrhages at birth, excluding those desperate cases in which there are massive hemorrhages, fall into this group.

Major operative procedures are recommended only in selected cases because of the high mortality which discourages all effort, resulting in the attitude, still too frequently encountered, that a child with a hemorrhage is so likely to be a defective that it is better for it to go

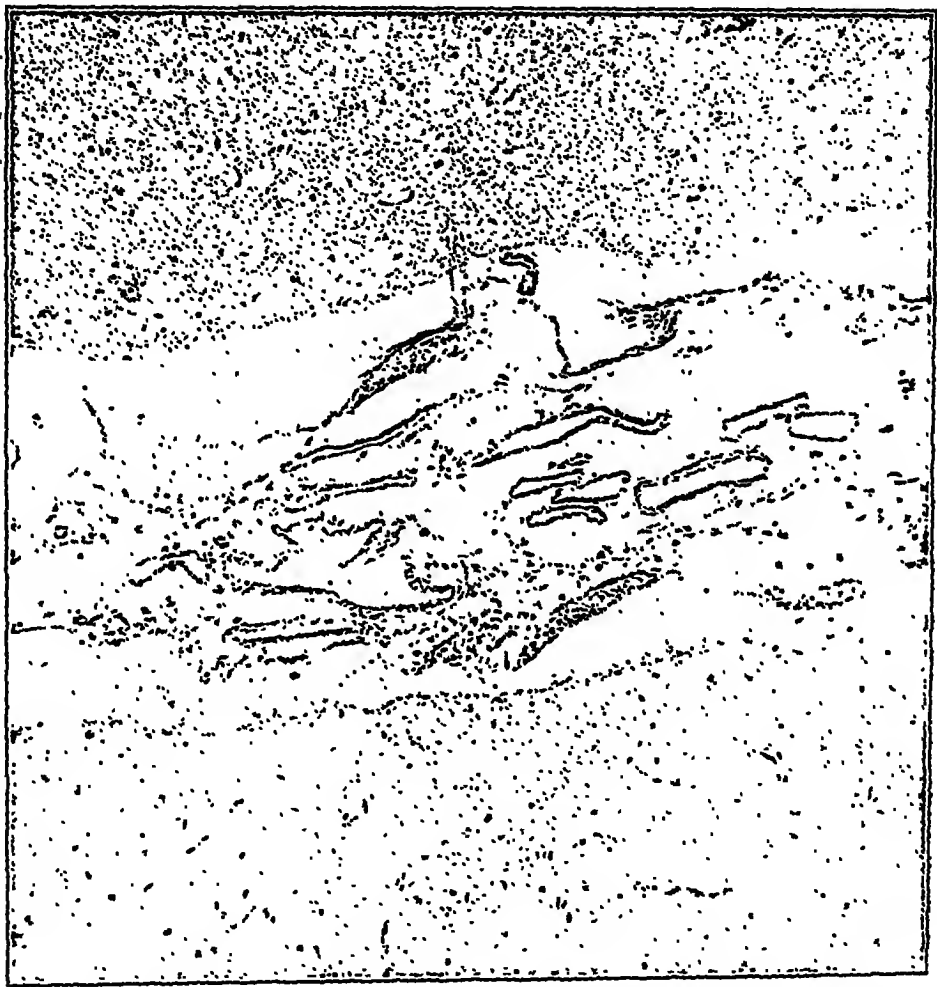


Fig. 29 (case 12).—Pia-arachnoid deep in a sulcus on the drained side in marked contrast to that shown in figure 28 corresponding to the gross changes in figures 24 and 25.

untreated with the hope that it will succumb. This is unfair in that it does not give the child a chance, and especially because many of the untreated survive with a poor chance for normal cerebral development. A good example of this was seen in a child who had had severe convulsions immediately after birth. The diagnosis of cerebral hemorrhage was made, and there was a stormy course for a month, during which time little hope of recovery was maintained. After a few weeks the

child had apparently recovered, but at the age of  $3\frac{1}{2}$  years, a general convulsive seizure was followed by other seizures at intervals of a few months.

General muscle rigidity is a prominent sign in neglected cases and usually starts when the acute signs of cerebral irritation cease.

*CASE 14.—Cerebral irritation when a few days old. Muscular rigidity at 1 month, which increased until treatment, lumbar puncture, was instituted at age of 2 months. Condition satisfactory when child was 6 months old.*

Baby P. Z., when a few days old had had a seizure, with marked cyanosis. When the child was 2 weeks old the mother noticed postcervical rigidity. At the age of 1 month there was general rigidity, and the head was drawn back to such an extent that the child could not lie in the dorsal position and could be raised from a lying to a sitting position by lifting the head (fig. 30). Because the eyes were rolled upward and did not follow an object, the mother also feared he could not see. Repeated lumbar punctures, fourteen in all, over a period of four months, were followed by satisfactory disappearance of the rigidity.

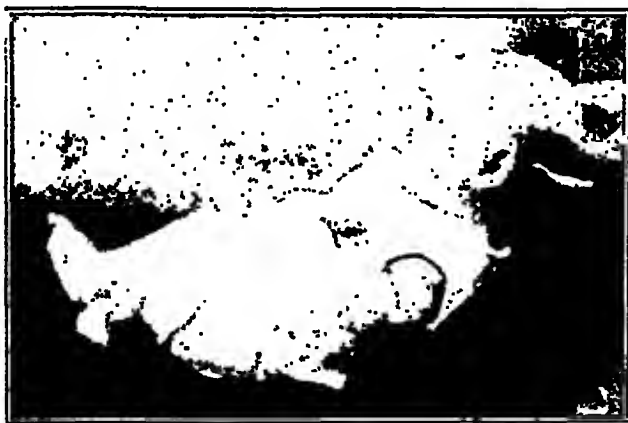


Fig. 30 (case 14).—The postcervical rigidity permitted the child to be raised to a sitting position by lifting the head (illustration taken from a moving picture film).

From this time, the mental and physical condition of the child did not cause concern. The photograph (fig. 31) was made when the child was 1 year of age to show normal muscle control.

The history of cerebral irritation during the first few days of life and the fact that improvement follows lumbar punctures differentiates these patients from the large group of children with spasticity resulting from developmental defects.

One child came under observation at the age of 9 years. This child, with her twin had had a normal birth, and at the age of 4 weeks was examined by the pediatrician, who told the mother that the patient was the better of the twins because of her ability to hold her head and spine erect. This probably indicated the early rigidity of a chronic meningitis; the mental and physical development of the patient, not so good as that

of the other twin, merged into a state of epilepsy at the age of 9 years. The head of the child had the appearance of a slight degree of hydrocephalus, and this fact was borne out by the roentgenogram of the air filled ventricles.

In a few cases, lumbar puncture will not control the symptoms, and a more complete and thorough drainage must be established through a decompression or osteoplastic flap.

*CASE 15.—Cerebral irritation at age of 1 week. After repeated lumbar punctures, all symptoms disappeared, except muscular rigidity, which improved during a period of subtemporal drainage but returned when drainage ceased. An osteoplastic bone flap followed by drainage entirely relieved the condition.*



Fig. 31 (case 14).—Normal muscle control when a little more than 1 year old (illustration taken from a moving picture film).

E. S., had had a convulsion on the seventh day after birth, and there was bulging of the fontanel. Lumbar puncture revealed blood-stained cerebrospinal fluid, diminished the bulging of the fontanel, and the convulsions ceased. Repeated punctures, six in all, until the age of 6 weeks, improved only temporarily the state of rigidity and the tension of the fontanel. At this stage, a more radical procedure was deemed necessary; an opening was made in the right subtemporal region, and a small rubber tissue drain was inserted. As long as drainage of cerebrospinal fluid continued, the condition of the child was satisfactory, but soon after the drain was removed, on the ninth day after operation, the tension and rigidity returned. The mother expressed anxiety over the condition of the child as compared with her two other normal children at this age. On the seventy-second day after birth, a right osteoplastic bone flap was done with the

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hope of draining more thoroughly the subarachnoid space. When the pia-arachnoid overlying the hemisphere was exposed, a low grade meningitis similar to that seen in the dogs was found. Drains were inserted over the cortex, and the dura was closed loosely. The rigidity gradually diminished and disappeared. The fear of the mother that the child would be backward, entirely subsided as normal mental and physical development (fig. 32) progressed throughout the first months after the operation. The child is now 4 years old and is quite like her brother and sister.



Fig. 32 (case 15).—Patient at the age of about 16 months showing an active, alert child.

Six of the twenty-six puppies injected had a rather marked degree of ventricle dilatation associated with chronic meningeal thickening and cortical scarring. The dilatation did not progress to an extreme degree and was associated with an excess of fluid over the cortex, which leads to the belief that the cerebrospinal fluid blocking was due to interference of absorption rather than to a blocking at the basal foraminae.

The two following cases in which the patients had slight enlargement of the ventricle and a large amount of fluid over the cortex with clinical evidence of hydrocephalus are of this type, although the cerebrospinal fluid blockage is different from that seen in case 1.

*CASE 16.—Cerebral trauma at the age of 2 months. Indefinite cerebral symptoms with gradual enlargement of the head until 8 months of age when examination showed slight enlargement of the ventricles and a large amount of fluid over the cerebral cortex.*



Fig. 33 (case 16).—Large amount of air over the cerebral cortex with only slight dilatation of the cerebral ventricles. The air was introduced through a lumbar puncture needle after the withdrawal of a large amount of fluid.

Baby W. W., fell from his crib at the age of 2 months. Little attention was paid to the injury, but during the following weeks the child was listless and inactive. At the age of 8 months, he was unable to hold up his head. When examined by me at the age of 9 months, the circumference of the head was 45.5 cm., the sutures were separated, and the fontanel was large and tense, giving the child a typical hydrocephalic appearance. A large amount of cerebrospinal fluid was withdrawn through a lumbar puncture needle, and air was injected (figs. 33 and 34). The illustrations show a large amount of air over the cerebral cortex with only slight dilatation of the ventricles. Repeated lumbar punctures failed to control the symptoms. Because of the long duration and the

advanced stage of the condition, so little was promised the parents that they declined operation. The child is now 2½ years old and is entirely helpless.

**CASE 17.**—*Small amount of blood in the cerebrospinal fluid at birth. Early cerebral irritative symptoms and during the third month evidence of hydrocephalus. Ventricles only slightly enlarged but a large amount of fluid over the cerebral cortex. Condition corrected by osteoplastic bone flap with free drainage of cerebrospinal fluid on one side and decompression with free drainage on the other side.*

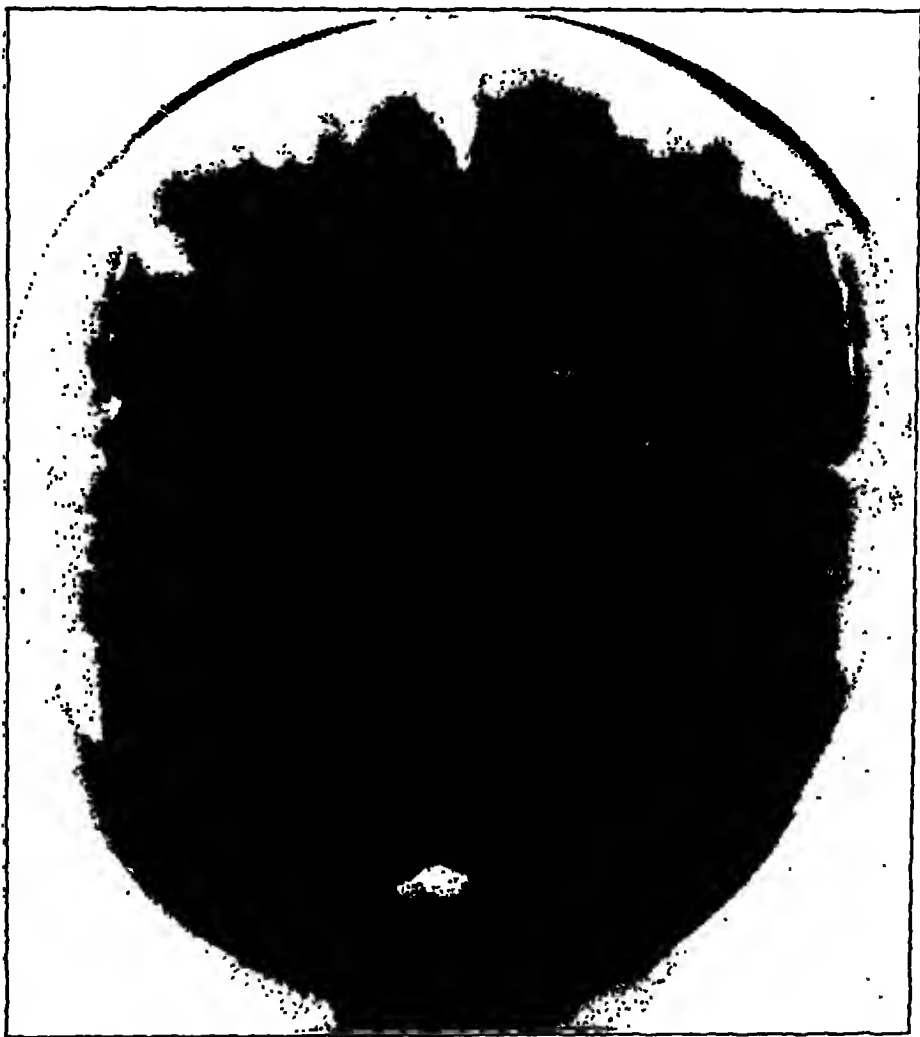


Fig. 34 (case 16).—Anteroposterior view also showing a large amount of air over the cerebral cortex with wide sulci.

Baby V. D., was delivered with high forceps after slow labor. Immediately after delivery, the condition was satisfactory. Later in the day, there was slight twitching of the hands and feet with some cyanosis. For the next forty-eight hours the child cried a great deal and refused to nurse, and its temperature ranged as high as 103 F. Lumbar puncture on the third day revealed cerebrospinal fluid with a pale yellow tinge. Because of the mild degree of twitching and the fact that the fluid was yellow on the third day, a favorable prognosis was given, as



it was believed the small amount of blood would be absorbed. Another puncture was advised to check the condition of the cerebrospinal fluid before the mother and the baby were discharged from the hospital. On the seventeenth day after birth, I examined the child again; the circumference of the head was 39 cm., the veins of the scalp were dilated, especially those from the bregma over the frontal region, the fontanel was tense, and the sutures were separated. Lumbar puncture revealed a more deeply yellow-tinged cerebrospinal fluid than at the time of the puncture two weeks previously. Three days later, the circumference of the head had increased 5 mm., and the cerebrospinal fluid pressure was 180 mm. of water. The appearance of the child was now definitely that of one with a



Fig. 35 (case 17).—Air injected through a lumbar puncture needle after the withdrawal of cerebrospinal fluid is shown in the wide sulci and over the cortex. The ventricles not shown in the print were slightly dilated.

beginning hydrocephalus, and it was determined to perform punctures at short intervals. Twelve additional punctures at intervals of from two to five days were made. When the child was 7 weeks old, air was introduced through a lumbar puncture needle, and the roentgenogram showed wide sulci, an abnormally large space between the cortex and the dura and a slight enlargement of the ventricles indicating an excessive amount of cerebrospinal fluid (fig. 35). At the age of 9 weeks, in spite of the lumbar punctures, the circumference of the head was 42 cm., the fontanel was larger, the sutures were separated, the

veins of the scalp dilated, and the head was heavy, requiring support when the child was picked up.

At this time, an osteoplastic bone flap was made uncovering a large part of the right cerebral hemisphere. The pia-arachnoid was definitely thickened. The cortical veins were engorged, and the arachnoid over the sylvian fissure and the sulci was literally distended with fluid. When the membrane over the sylvian fissure was punctured, fluid slowly escaped as though seeping from a mesh. The wound was closed with a drain. For several days after the operation, there was free drainage of cerebrospinal fluid. Three weeks after operation, the circumference of the head was 41.5 cm., the fontanel was soft, scalp veins were not overfilled, and the child had regained some control of the muscles of the neck but was still unable to hold the head erect. The condition continued to improve for several weeks, when the tension was again increased and the head began to enlarge. Frequent lumbar punctures were tried, but failed to control the con-



Fig. 36 (case 17).—Photograph of patient at the age of 13 months. The head is larger than normal, but the sutures are closed, and there is no evidence of increased intracranial tension.

dition, and at the age of 19 weeks an opening was made in the left temporal region and drains were inserted. From this time on, the fontanel gradually decreased in size and the circumference increased only at the normal rate. The condition of the child at the age of 13 months is shown in figures 36 and 37. Except for slight enlargement of the head, the physical and mental condition is entirely normal.

The clinical course in this case, different from that of the other groups described, typifies what happens infrequently, but which I believe is nevertheless a definite clinical entity. Through the irritating effects of the blood in the cerebrospinal fluid, there is interference with the

absorption of the fluid. Puncture of the dura as by lumbar puncture in the milder cases or by an extensive opening as a bone flap in the more severe types unblocks at some point, and absorption is reestablished.

That the opening of the dura has an influence on this type of case was first brought to my attention in a child born after a prolonged and difficult labor, who was normal for a period of two weeks, after which



Fig. 37 (case 17).—Lateral view of the head at the age of 13 months.

there was rapid enlargement of the head. It was thought that there was a blood clot over the cerebral cortex, and several small openings were made through the skull and dura. A clot was not found, and the wounds were closed tightly. From the time of the operation, the head ceased to enlarge. An explanation of this was not had at the time, but I now believe that the mere opening of the dura helped rid

the subarachnoid space of the irritating cerebrospinal fluid. This child is now 13 years of age, has always been backward, and since the age of 5 years, has had convulsive seizures. Early complete subarachnoid drainage, would perhaps, have given this child a much better chance.

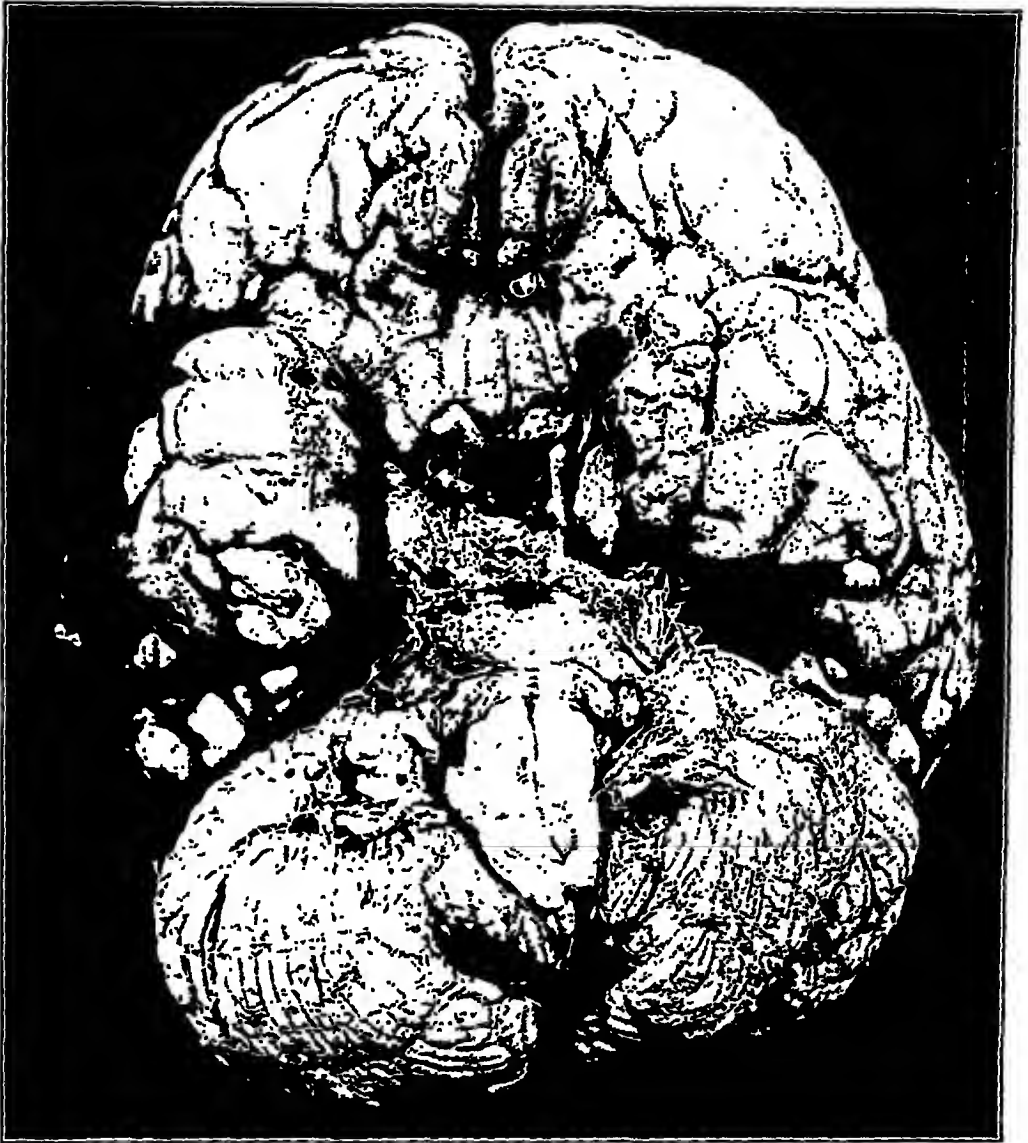


Fig. 38 (case 18).—Meningeal thickening twenty days after cerebral trauma with bloody cerebrospinal fluid.

In 1903, Dr. William G. Spiller<sup>4</sup> called attention to the importance of cases of cerebral trauma without displacement of bone in which a blood clot, even though small, is present, and in spite of the early disap-

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4. Spiller, W. G.: *Traumatic Lesions of the Brain in Their Relation to Operation*, Internat. Clin. 4:102, 1923.



Fig. 39 (case 18).—Section of the meninges from the base showing meningeal thickening and cell infiltration.

pearance of symptoms of compression, the patient is in danger of becoming epileptic or developing traumatic insanity.

In 1904, Dr. Adolf Meyer<sup>5</sup> in his discussion of mental patients who had previously had a cerebral trauma remarked: "Whether the cranium is fractured or not means relatively little. It would seem, however, that for chances concerning life, a relatively extensive destruction of the skull is rather more favorable than otherwise."

In the light of my experimental work the drainage of cerebrospinal fluid seems to be of paramount importance, and I am inclined to feel that the danger of immediate and late symptoms is lessened in the compound cases in which the dura is opened allowing a free escape of blood and cerebrospinal fluid.

Dr. Harvey Cushing,<sup>6</sup> in his paper in 1907, calls attention to the advisability of decompression and drainage. This marks the beginning of a type of cranial surgery which has proved very useful. Confusion in the selection of patients for operation occurs because of failure of surgeons to consider carefully the underlying lesion in attempting to determine whether the patient should or should not be treated by decompression. For instance, in some clinics, an attempt has been made to settle the question by operating on a given number of consecutive "fractured skulls" and comparing them with a second series, none of which were subjected to operation. The outcome of these discussions has resulted in the conviction that there is a type of case in which the patient may recover spontaneously, but the recovery can be speeded and a more simple postoperative course can be assured by drainage of cerebrospinal fluid. It has further been recognized that in many of these cases the bloody cerebrospinal fluid can be drained through repeated lumbar punctures, thus avoiding the more radical procedure of decompression and drainage. Here again the pendulum may swing too far, and care must be taken not to overlook the case in which lumbar puncture will not suffice and a decompression or even a bone flap is required.

The importance of bloody cerebrospinal fluid as a result of injuries without displacement of bone is shown in the following fatal case in which the symptoms immediately after the injury were slight. During the second week, meningeal irritative signs gradually developed to a serious stage, and the patient died during the third week in spite of lumbar puncture and late decompression.

*CASE 18.—Late appearance of symptoms following the escape of blood in the cerebrospinal fluid. Decompression delayed until the sixteenth day after the*

5. Meyer, A.: The Anatomical Facts and Clinical Varieties of Traumatic Insanity, *Am. J. Insan.* 60:373, 1904.

6. Cushing, A.: A Discussion of some Immediate and some Remote Consequences of Cranial Injuries, Based on Three Clinical Histories Which Illustrate the Extradural, Subcortical, and Intermenigeal Types of Intracranial Hemorrhage, *New York M. J.* 85:214, 1907.

*accident accomplished nothing. Section of the meninges showed marked meningeal reaction.*

G. G., a man, aged 35, was thrown from an automobile and struck his head. He went to his home, and his condition did not cause any concern until the end of the first week, when there was headache and mental confusion with slight elevation in temperature. He was treated at home for several days, during which time the symptoms increased. When the patient was admitted to the hospital fourteen days after the accident, the pulse rate was 60 per minute, there was postcervical rigidity, a positive Kernig sign, some delirium, severe headache and beginning choking of the disks. Lumbar puncture showed yellow-tinged cerebrospinal fluid. Following the puncture, the patient was more comfortable. A second lumbar puncture was made after an interval of six hours, and a third, twenty-four hours later. The symptoms increased, and a right subtemporal decompression was performed forty-eight hours after admission, at which time the patient presented the appearance of one suffering from advanced meningitis. When the dura was opened, there was bulging of the cortex and only a small amount of cerebrospinal fluid escaped, indicating that the condition had reached the stage of cerebral edema. The pia-arachnoid was opaque, but there was no evidence of exudate. Drains were inserted over the cortex. Following the operation, there was scant drainage of cerebrospinal fluid, and the condition grew worse until death four days later. Autopsy revealed a film of blood mixed with cerebrospinal fluid throughout the subarachnoid space. The meninges at the base were thickened (fig. 38) and blood-stained. A section of the meninges from this area (fig. 39) showed the reaction.

In this case, the disturbance at the time of admission to the hospital is now believed to have been due to edema of the brain which, no doubt, followed a stage in which there was an excess of fluid in the subarachnoid space. The period for lumbar puncture had passed, and a more radical procedure for complete drainage was indicated.

In the following case, lumbar puncture was not made, as there was evidence of "medullary disturbance." On the fourth day, a convulsive seizure occurred, and because of the serious condition following it, a right subtemporal decompression was performed.

*CASE 19.—Cerebral trauma with a general convulsive seizure and complete loss of consciousness on the fourth day.*

J. G. N., a married woman, aged 40, was injured in an automobile accident, receiving a blow in the right frontal region. She was admitted to the hospital one hour later, when there was some bleeding from the nose and right external auditory canal; the blood was not mixed with the cerebrospinal fluid. In the beginning she was unconscious; this condition improved, but mental confusion continued. In spite of evidence of "medullary disturbance" with marked increase in the deep reflexes, clonus and a bilateral Babinski sign, the condition did not seem alarming until the afternoon of the fourth day, when she had a convulsive seizure with cyanosis, a severe drop in the blood pressure, pulse and respiratory rate, the latter reaching 10 per minute. Following the seizure, there was complete loss of consciousness for four hours, at which time a right subtemporal decompression and free drainage of cerebrospinal fluid were accomplished. Following the operation there was prompt recovery, and the patient was discharged on the twelfth day, at which time there was some blurring of vision and slight mental confusion. When examined recently two and a half years after the accident, the patient was normal.

The sudden onset of symptoms in a man four days after an accident is shown in the following patient:

*CASE 20.—Cerebral irritation with bloody fluid four days after trauma promptly relieved by lumbar puncture.*

J. S., a man, aged 34, was admitted to the hospital immediately after an injury in the right frontal region of the head. There was little headache, and the temperature ranged from normal to 100 and the pulse rate from 70 to 100 per minute for the first four days. During the evening of the fourth day, the patient complained of severe neuralgia-like headache; he vomited, and the temperature registered 97 F. with a fall in pulse rate to 60 per minute. Lumbar puncture revealed bloody cerebrospinal fluid. Later, lumbar puncture showed the cerebrospinal fluid gradually returning to normal, and all symptoms disappeared.

The symptoms in this patient were due to a gradually increasing meningitis. It is unwise to disturb a patient who is apparently doing well, but an early lumbar puncture would have prevented the severe reaction in this case. One year after the accident this patient had indefinite symptoms, such as headache and dizziness of a mild degree.

The late appearance of signs and symptoms is shown in the following case:

*CASE 21.—Cerebral trauma with bloody cerebrospinal fluid. Gradually increasing symptoms for two weeks; gradual disappearance of symptoms following repeated lumbar puncture.*

W. C., a man, aged 20, received a severe blow over the right frontal region of the head while playing football. After a few moments he continued playing, and in spite of a slight headache, worked the following day and attended a dance during the evening. He complained slightly, and forty-eight hours after the injury consulted his family physician because of mild headache and occasional vomiting. Two weeks after the date of the injury, I saw him because the pulse rate was ranging from 48 to 52 per minute. He was rather dull when left alone, but when stimulated, would talk and seemed entirely normal. He said there was no real headache, but a feeling of tightness and some tenderness of the scalp. The examination showed a rather listless youth with speech distinct but slow. The disks showed definite changes from the normal, with a mild degree of choking. Three hours after the puncture, the patient said he felt different. The dull feeling in the head was gone, and he was more alert. Lumbar puncture twenty-four hours later showed the same yellow fluid. Two weeks after the first puncture, the fluid was almost entirely clear. Twenty-six days after the first puncture, because of nervousness, another puncture was made and the fluid was colorless. The patient did not complain of headache, and returned to his work.

*CASE 22.—Cerebral trauma with symptoms two weeks later, but patient not treated until one month after the accident. Well marked meningeal reaction with evidence of increased intracranial pressure, relieved by decompression and drainage.*

R. S., a boy, aged 12, fell from a fence and struck his head in the left parietal region. There was nausea and vomiting and some headache for two days. After that time he seemed normal, but later developed an internal squint of the right eye and complained of photophobia. He played normally for two weeks, when there was some drowsiness, and he was inactive for the greater part of the next two weeks. When examined four weeks after the accident, there was marked choking of the disk, paralysis of the right external rectus and stupor, but he could



be aroused to carry out simple commands. The pulse rate was 60 per minute, the leukocytes numbered 11,000, and a suggestive Kernig sign was present. The roentgenogram showed a linear fracture of the right parietal region. A right subtemporal decompression was performed, and drains were inserted. The dura was tense, and when opened there was free drainage of cerebrospinal fluid. The following day, the external rectus muscle was less weak. All symptoms gradually disappeared during a period of three weeks, when the patient was discharged.

**CASE 23.**—*Cerebral trauma with delay of serious symptoms for seven weeks. Late appearance of convulsions and partial hemiplegia at first led to the diagnosis of apoplexy. Because of history of trauma, decompression with drainage was done.*

F. S., a man, aged 55, fell on his head while climbing an ice-covered wooden fence. He was at first dazed, but walked home. Three weeks later, he had vague symptoms for which he consulted a physician. Seven weeks after the accident, he returned home after attending church, walked upstairs to retire for the night and had a convulsive seizure, after which there was headache and vomiting, slight weakness of the right side of the face and of the arm and mental confusion. The symptoms continued, and I first saw him four days later. Examination at that time revealed the patient in stupor; the pulse rate was slower than normal, there was a mild choking of the disks and slight weakness of the right side of the face and of the right arm. With the history of the sudden onset four days before, the diagnosis of cerebral hemorrhage was made. In discussing the case with the patient's wife following the consultation, she remarked that the patient had never been the same since he fell over the fence. This was the first mention of the accident, which, because of the interval of seven weeks, had not been thought to have any connection with the present condition, and was not mentioned by the other members of the family who had originally given the history. Careful questioning revealed that the patient had had vague symptoms and had consulted a physician for slight headache three weeks after the accident. It was then concluded that the symptoms were, perhaps, due to the accident, and exploration was advised. During the period of twenty-four hours in the hospital before the operation, the temperature ranged from 100 to 101 F., and the pulse rate from 45 to 65 per minute. There was beginning choking of the disks, weakness of the muscles of the right side of the body and stupor. Decompression was performed and an opaque arachnoid with distention of the cortical vessels was seen. A drain was placed beneath the dura and the wound was closed. Following the operation, there was a gradual falling of the temperature, which reached normal on the eighth day after admission. All symptoms improved, and the patient was discharged from the hospital on the thirty-third day. Ten years have passed since the operation, and the patient is living and well.

Just what part syphilis plays in spontaneous cortical hemorrhages with extravasation of blood into the cerebrospinal fluid has been variously stated.

**CASE 24.**—*Cerebral syphilis with a sudden hemorrhage into the cerebrospinal fluid followed by severe pain and delirium. Gradual improvement of symptoms for five days. Lumbar puncture on the fifth day showed yellow fluid. Rapid improvement following lumbar puncture.*

G. J., a married man, aged 37, while driving his car on April 27, 1923, was suddenly seized with severe headache and vomiting. He was taken to the office of a physician in a state of collapse. For one week following the onset of symptoms, he was wildly delirious. There was elevation in temperature, and the pulse rate was rapid. He was admitted to the hospital five days after the attack,

complaining of headache and pain in the extremities. Lumbar puncture made the next day revealed slightly bloody cerebrospinal fluid; another a week later showed clear yellow cerebrospinal fluid. The patient was discharged from the hospital eleven days after admission, the stupor following his delirium having cleared up. The Wassermann reaction of the blood and cerebrospinal fluid was positive, and the patient was treated for syphilis. It is now almost five years since his discharge from the hospital, and there has not been any recurrence of the symptoms. The symptoms in this type of case are due to meningeal irritation. The fact that this patient had syphilis and had refused thorough treatment was known to his physician; he, therefore, attributed the mental upset to this, and was planning to have the patient committed to an institution. As the condition improved after five days, the patient was admitted to a general hospital, where it was decided the mental condition was due to the blood in the cerebrospinal fluid.

Arteriosclerosis and hypertension play an important rôle, and care must be taken to differentiate cases in which the symptoms are due to escape of blood into the cerebrospinal fluid from those due to a hopeless subcortical clot. The first intimation of the hopeful type is found when the patient shows evidence of meningeal irritation ranging from severe headache and postcervical pain to rigidity and convulsive seizures with elevations in temperature and pulse rate. In either type there must be some blood in the cerebrospinal fluid; but a lumbar puncture with the withdrawal of even a small amount of fluid will cause improvement in patients with the simple type and will have a bad influence if any on patients with subcortical clot.

*CASE 25.—Cerebral arteriosclerosis with bloody cerebrospinal fluid and severe cerebral irritative symptoms which were relieved by repeated lumbar punctures.*

J. H. S., a married man, aged 54, after hurriedly driving his car, became slightly confused mentally and thick in his speech. There was a slowly increasing stupor, which was never deep. Two hours after the onset, the patient had a general convulsive seizure; during the next ten hours, he had three more, at which time there was slight weakness of the right side of the face and of the right arm. The blood pressure was 200 systolic and 130 diastolic and later dropped to 190 systolic and 90 diastolic. When I examined the patient the first time, at 4 p. m., the following day, twenty hours after the onset of the trouble, there was partial aphasia and slight weakness of the right arm and of the right side of the face, and the reflexes were greater in the right than in the left upper extremity. There was stupor and mental confusion. The patient seemed to be uncomfortable because of headache. On lumbar puncture, bloody cerebrospinal fluid was withdrawn. Following the puncture, the patient was more comfortable. Repeated punctures were made until the fluid was clear one week after the onset, and the patient gradually improved, though the aphasia never entirely cleared up. The patient is still living, two and one half years later, the blood pressure has remained high, and he now presents the usual picture of cerebral arteriosclerosis.

*CASE 26.—Bloody cerebrospinal fluid perhaps due to rupture of an arteriosclerotic cerebral vessel. On admission of patient to hospital one week after sudden onset, the signs and symptoms suggested tumor of the brain. Repeated lumbar punctures followed by disappearance of all signs and symptoms.*

Mrs. C. G., aged 56, was suddenly seized with severe pain in the head. Within twenty-four hours the patient was in coma which lasted for several hours. Severe headache with paroxysmal attacks of agonizing pain and loss of consciousness

occurred several times daily. When admitted to the hospital one week after the onset, she showed bilateral choked disks, bilateral abducens weakness and slight weakness of the left side of the body, including the face. There was postcervical rigidity and positive Kernig sign. Dizziness was troublesome, especially when the position was changed. The diagnosis of cerebellar tumor was made, but because, of the sudden onset, postcervical rigidity, positive Kernig sign, and slight elevation in temperature and increased pulse rate, the immediate cause of the symptoms was believed to be due to the escape of blood in the cerebrospinal fluid. A lumbar puncture was made, and bloody cerebrospinal fluid was obtained. The condition was followed by immediate temporary improvement in the symptoms. Repeated lumbar punctures, nine in all, brought about a subsidence of symptoms, though the disturbance of the eye movements persisted for three months. Convalescence was slow, but the patient is living and well and free from symptoms with a blood pressure of 160 fifteen months after the illness.

Lumbar puncture in the presence of choked disk due to tumor is an extremely dangerous procedure; on the other hand, when there is an excess of cerebrospinal fluid, a lumbar puncture is not dangerous but offers relief. In this case, the possibility of tumor as the underlying cause of the blood must be considered, but there can be no doubt as to the blood having caused the immediate symptoms, and the interval of one year without symptoms makes the diagnosis of tumor unlikely. A similar case recently came under observation.

*CASE 27.—Bloody cerebrospinal fluid with increased intracranial pressure and other signs suggesting tumor of the brain. Gradual improvement of symptoms as lumbar punctures were made.*

C. C., a married man, aged 46, while at work was suddenly seized with severe pains in the head and was immediately taken to the hospital in an unconscious condition. There was postcervical rigidity and a positive Kernig sign. When he was examined, twenty-four hours after the onset of the trouble, the pulse was slow and the disks indicated an increase in intracranial pressure. Lumbar puncture revealed a bloody cerebrospinal fluid. In this case, the early change in the disk and the slow pulse rate with slow clearing up of the symptoms after puncture made one suspicious of something more than a little blood mixed with the cerebrospinal fluid, perhaps a tumor or large hemorrhage with some leakage into the subarachnoid space. Three weeks after the onset of the symptoms, the fluid was almost entirely clear; the patient was still somewhat confused, but gradually improved, following much the same course as that noted in case 24. It is now three months since the onset, and the patient is gradually improving; all signs and symptoms have disappeared, except dizziness and some unsteadiness of gait.

#### SUMMARY

Short clinical histories of twenty-seven patients with bloody cerebrospinal fluid are presented. In most of the cases, the blood in the fluid resulted from trauma, and the effect of the blood is shown in the acute, subacute and chronic stages.

In two cases, the blood was due to congenital venous anomalies, and in one case to a tumor of the brain present at the time of birth.

Five patients ranging in age from 12 to 44 years had aneurysms of the anterior cerebral arteries.

In four of the patients who recovered, the exact underlying causes could not be determined, but arteriosclerosis was the most probable factor.

#### COMMENT

The material has been collected for the purpose of demonstrating the acute and chronic changes in the central nervous system following the introduction of blood in the cerebrospinal fluid.

Cases in which there were meningeal irritations due to a free mixture of the blood with the fluid have been selected, and the discussion does not include cases in which the patients had large blood clots.

The symptoms immediately following the escape of blood into the cerebrospinal fluid depend on the amount of blood and vary from slight headache to severe pain with convulsive seizures and loss of consciousness. The most important signs and symptoms in patients with a small quantity of blood usually appear after an interval of a few days and are due to the reaction of the meninges. This state is characterized by headache of a neuralgic type, delirium, mild elevation in temperature, slight increase in pulse rate, postcervical rigidity and a positive Kernig sign. These symptoms may gradually subside as the blood is absorbed. In adults, complete recovery may take place, but infants presenting the early symptoms, if allowed to go untreated, frequently develop rigidity of the muscles and epilepsy. If the early symptoms progress, the signs of cerebral edema with evidence of marked increase of intracranial pressure may appear and may result in death.

An analysis of the signs and symptoms due to bloody cerebrospinal fluid impresses one with the importance of recognizing the condition, because the diagnosis in these patients may be confused with that in almost any of the common lesions of the brain from meningitis to tumor of the brain. In some cases, the disturbance due to the blood in the cerebrospinal fluid must be cleared up before the primary lesion can be diagnosed.

Treatment depends on the stage of the disease and should be carried out with the view of removing the irritating blood and preventing or relieving the meningitis. Absorption of some blood always takes place, but this is associated with meningeal thickening which may cause a block in the channels through which the fluid is returned to the blood stream. Treatment, therefore, has to do with the drainage of fluid which may be accomplished through lumbar puncture or the more radical procedure of decompression or even a bone flap. Some of the cases for this paper have been selected for the purpose of showing types suitable for the various procedures.

This work has been carried on under the direction of Dr. Adolph Meyer. Dr. Robert B. Wright assisted in the study of the specimens and Miss Cecelia Bisson made the illustrations.

# BILATERAL LOBAR ATELECTASIS

## REPORT OF A CASE WITH AUTOPSY OBSERVATIONS \*

R. P. BALL, M.D.

CLEVELAND

This is a report of a case in which bilateral lobar atelectasis was associated with acute pancreatitis (fat necrosis). The observations made at autopsy suggest a probable explanation for the collapse of the lower lobes of the lungs.

### REPORT OF A CASE

A woman, aged 48, who had enjoyed good health until October, 1925, developed symptoms of hyperthyroidism. A thyroidectomy was performed on Nov. 28, 1925. The gland showed slight hyperplasia. Preceding the operation, the basal metabolic rate was plus 56 per cent. In March, 1926, the basal metabolic rate was minus 21 per cent, and the patient showed other signs of hypothyroidism including obesity. After this time, thyroid extract was administered regularly.

Four months before her final admission to the hospital, the patient had intermittent colicky pains in the upper right quadrant of the abdomen, which were diagnosed as "gallbladder attacks." Three days before admission (Dec. 4, 1927), the patient had a severe persistent pain in the upper right quadrant of the abdomen, which became localized in the region of the gallbladder and was accompanied by vomiting. The pain was referred to the back and was described by the patient as being "between the shoulder blades." On December 7, the patient had a transient cyanosis which lasted for fifteen minutes and was characterized by rapid respiration and a feeling of impending danger.

On admission to the hospital, on December 8, the patient had a temperature of 38 C.; the pulse rate was 130 and the respiratory rate was 25. Physical examination revealed tenderness in the region of the gallbladder and a questionable tumor-like mass which appeared to be an empyema of the gallbladder. The lower lobe of the right lung was thought to be consolidated, and over the lower lobe of the left lung were heard numerous moist râles and tubular breathing. A diagnosis was made of empyema of the gallbladder with possibly bronchial pneumonia. Because of the serious condition of the patient, an exploratory operation was postponed.

The average white blood cell count while the patient was in the hospital was 16,000 per cubic millimeter. The red blood cell count was 3,400,000. Eighty-three per cent of the white blood cells were polymorphonuclear neutrophils. The urine was acid in reaction; the specific gravity was 10.10, and all specimens showed two plus albumin. There was no glycosuria and the microscopic examinations showed the constant presence of a few pus cells. A liver function test showed 1.2 mg. serum bilirubin. The blood sugar averaged 120 mg. per hundred cubic centimeters. Plasma carbon dioxide was 39 and the blood urea, 57. A culture of the sputum did not reveal pneumococci. A roentgenogram was reported as unsatisfactory (fig. 1), but because the patient was thought to have pneumonia there was some objection to making another roentgenogram.

On December 21, the abdominal tenderness became more generalized, and the abdomen appeared to be more distended than before. An exploratory

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\*From the Department of Pathology, Cleveland Clinic.

laparotomy was therefore performed on the patient without removing her from her bed. The operation was done under local anesthesia with procaine hydrochloride together with nitrous oxid-oxygen analgesia. An upper right rectus abdominal incision was made, and the peritoneal cavity was then exposed. The liver was found to be pushed over to the right and numerous adhesions between the anterior abdominal wall and the region of the falciform ligament were found. Many small, dull white, oval areas were scattered throughout the peritoneal cavity; these were more numerous on the omentum, a condition which is typical of fat necrosis. The lesser peritoneal cavity was distended with a pale red, serous fluid. An opening was made in order to drain the fluid, and a drain was placed in the region of the pancreas. Eight hours later, the patient ceased to breathe.

*Necropsy Report.*—An autopsy performed one hour post mortem revealed the following: The peritoneal cavity contained blood-stained serum and a blood



Fig. 1.—Bilateral lobar atelectasis; consolidation of the lower lobes.

clot. The falciform ligament was 4 cm. to the right of the midsternal line; the greater omentum was uniformly distributed over the intestines with the lower border at the pelvis. Numerous oval, dull white, discrete areas averaging 10 mm. in diameter were scattered throughout the omentum and peritoneal cavity; the tissue surrounding these areas was not discolored. On account of edema and of infiltration of the tissue surrounding the foramen of Winslow which produced mechanical obstruction between the two peritoneal cavities, the lesser peritoneal cavity did not communicate with the greater cavity. The lesser cavity contained about 3,300 cc. of blood-stained serous fluid in which were floating bits of debris.

When the sternum with the attaching costal cartilages was removed, the mediastinum was found in the midline. Both pleural cavities were clean. The dome of the diaphragm on the right was at the level of fourth rib, and on the left, at the level of the fourth intercostal space.

The pericardial cavity was clean. The apex of the heart was 10 cm. to the left of the midsternal line and at the fifth rib.



Fig. 2.—Lungs in case of bilateral lobar atelectasis. Note the relatively small lower lobes and the sharp line of demarcation of the atelectatic areas.

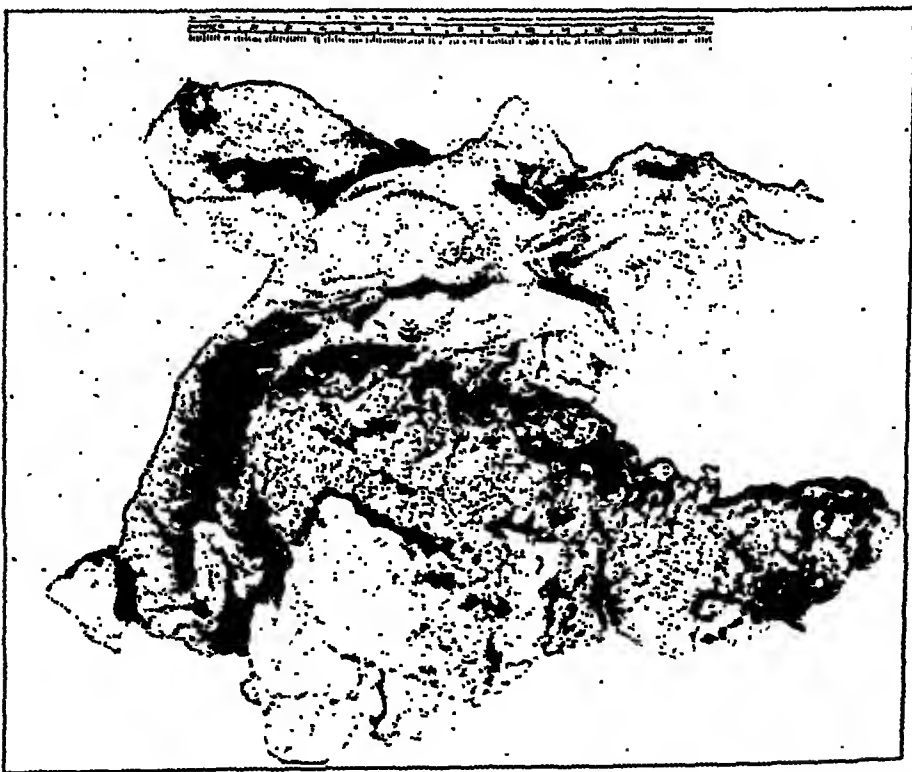


Fig. 3.—Pancreas with attached duodenum in case of acute pancreatitis—fat necrosis, associated with bilateral lobar atelectasis.



The left lung weighed 300 Gm., the right, 320 Gm. With the left lung in situ only a narrow margin of the lower lobe was visible. The upper lobe was of a pale bluish-gray cast with dull slate-colored mottling. The right lung in situ was similar to the left lung. The pulmonary artery was opened without disturbing the organs and was found to be normal. The trachea and the first division of the bronchi were opened and were found to be clean. The lower



Fig. 4.—Lobar atelectasis, showing obliteration of the alveolar spaces by apposition of the interalveolar walls;  $\times 160$ . Note that blood vessels are free from thrombi.

lobe of the left lung was limp, flabby and airless, and its pleural covering was clean and glistening except for a small area about 3 by 1 cm. which was covered with a loose fibrous adhesion. The cut surface of the lower lobe was homogeneous in appearance. A small amount of blood-stained material was obtained only on



continued scraping. The cut surface of the upper lobe was pale pinkish-gray and was moist. The right lung was similar to the left except that there was an atelectatic area at the base of the middle lobe which was identical in appearance with the lower lobe (fig. 2).

The pancreas was soft dark reddish-gray; it was friable and of about the same appearance throughout. On account of shaggy-lined crypts filled with friable, dark gray material, the surface was uneven (fig. 3).

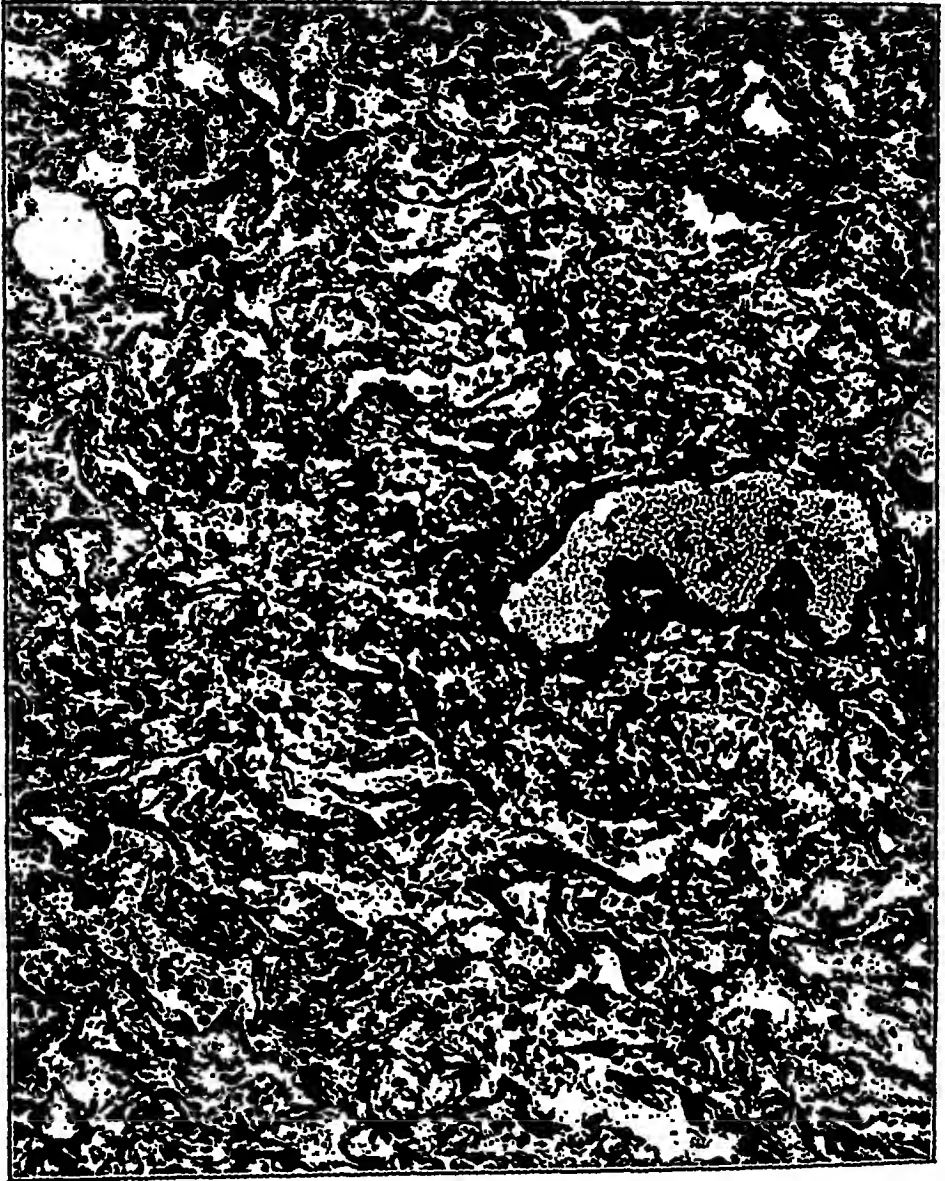


Fig. 5.—Lobar atelectasis, showing apposition of many of the interalveolar walls, and the presence of serum and red blood cells in the alveoli;  $\times 160$ . Note absence of thrombi in both arteries and veins.

The falciform ligament was 4 cm. to the right of the midsternal line. The lower border of the right lobe of the liver was 10 cm. below the costal margin in the right midclavicular line. The edges were slightly rounded and the surface of the organ was smooth. The cut surface showed normal lobular markings.

The serosa of the gallbladder was smooth and clean. The organ was slightly ballooned and was filled with dark tenacious bile containing numerous small soft yellowish faceted stones averaging 3 mm. in diameter. On squeezing the gallbladder, bile flowed from the ampulla of Vater.

*Microscopic Observations.*—Sections through the atelectatic area showed the interalveolar wall to be in apposition. Some of the alveoli of the lungs contained mononuclear leukocytes, serum and red blood cells. The bronchi contained mononuclear leukocytes. With the exception of the lining cells of the alveoli, which were more cuboidal, the alveoli were normal in appearance (figs. 3 to 5).

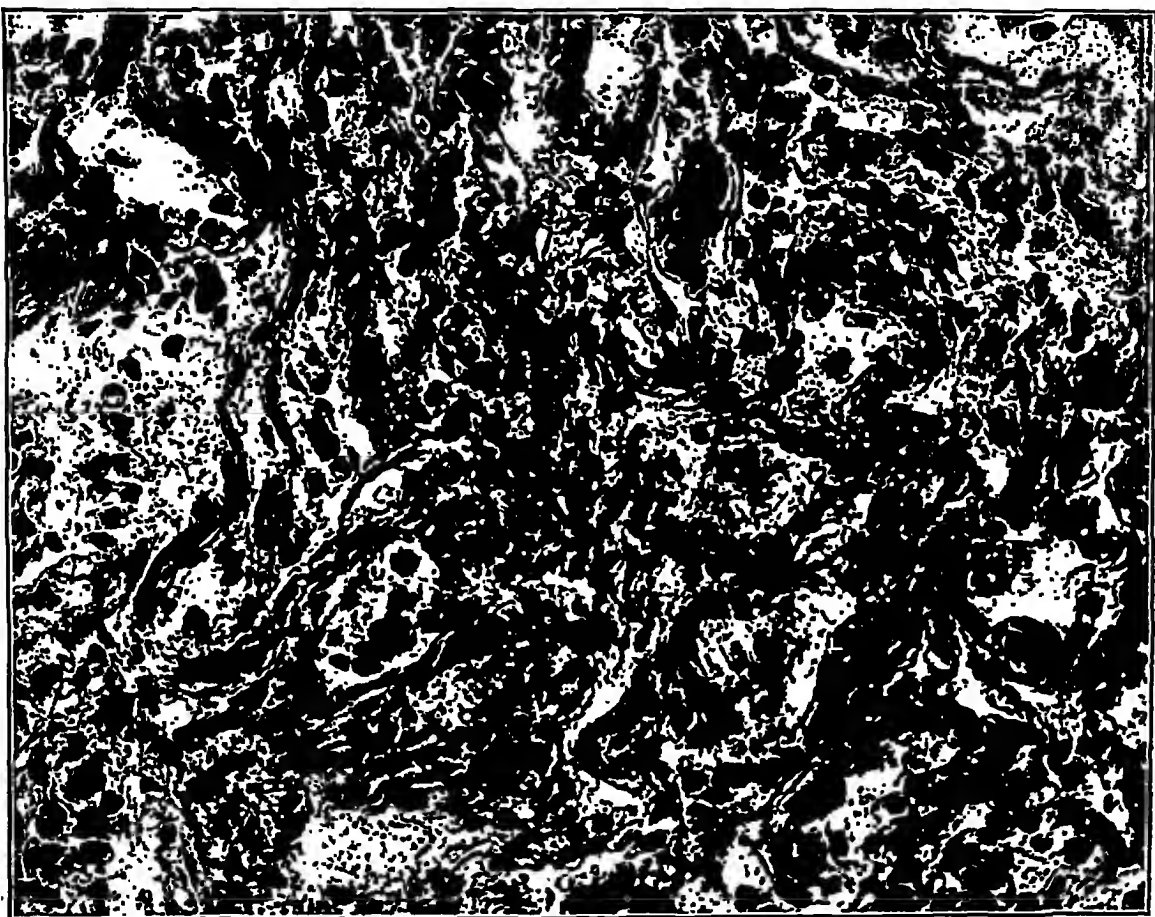


Fig. 6.—Lobar atelectasis, showing the lining cells of the alveoli have become cuboidal or rounded as the result of contraction of the alveoli;  $\times 250$ .

There were intact scattered islands of parenchyma in the pancreas which stained normally. The remaining tissue when stained presented a neutrophilic indistinguishable mass without histologic markings (necrosis). No leukocytic reaction was apparent except for an occasional clump of polymorphonuclear leukocytes at the periphery of the necrotic area (figs. 6 to 8).

*Anatomic Diagnosis (Gross and Microscopic):* The following anatomic diagnosis was made: (1) Acute pancreatitis (fat necrosis); (2) lobar atelectasis, bilateral; (3) cholecystolithiasis; (4) hydroperitoneum (ascites); (5) obstruction of the foramen of Winslow, and (6) recent laparotomy wound.

## COMMENT

The term atelectasis is used here to denote the condition of the lung in a collapsed state. Although the term atelectasis of the lung is usually used to designate the complete or incomplete failure of the lung of the new-born to expand, nevertheless, no other term describes collapse of the lung of unknown etiology as well, especially when the etiology of this condition appears to be a lack of expansion, as shown in the foregoing case.

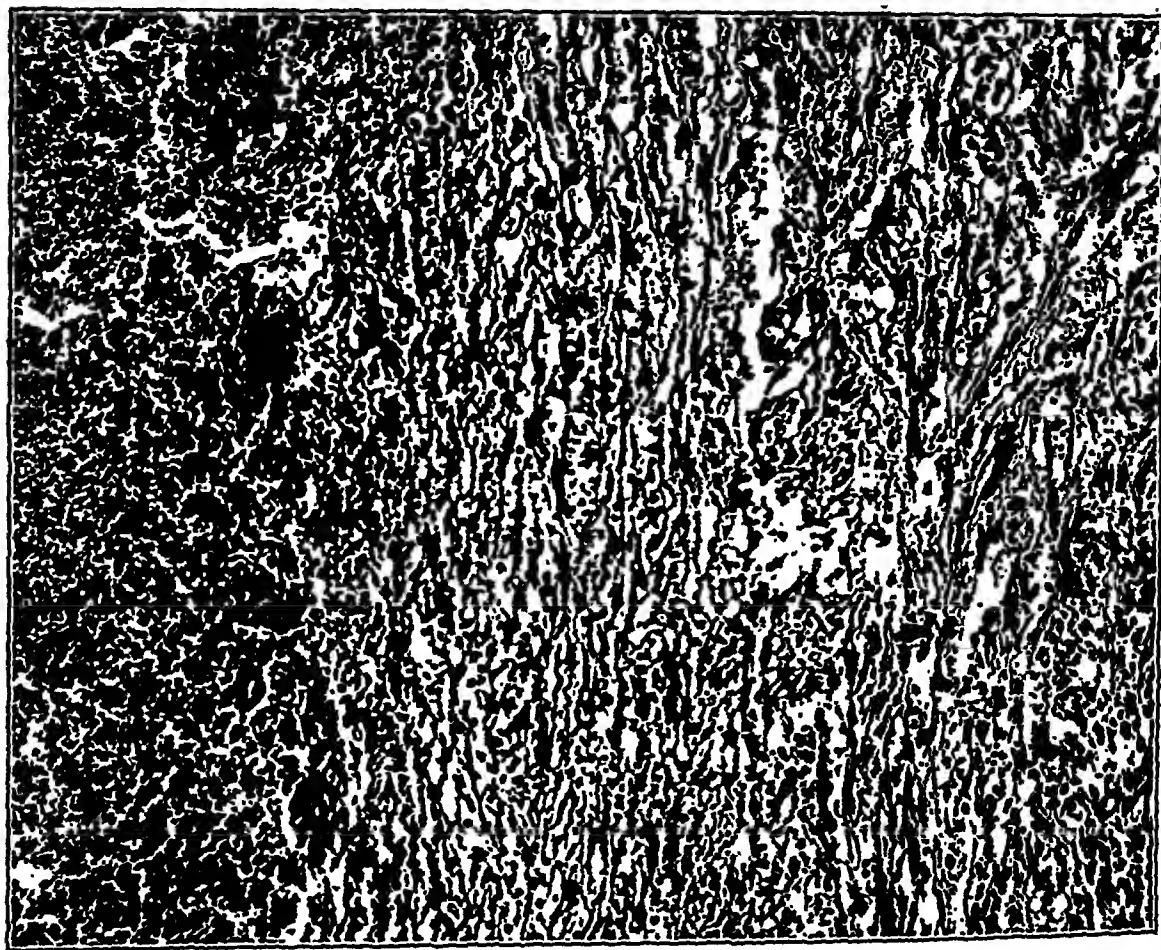


Fig. 7.—Acute pancreatitis—fat necrosis, showing absence of parenchyma and marked polymorphonuclear reaction;  $\times 160$ .

This lesion has never been experimentally reproduced except by ligating the bronchi. The use of plugs in a bronchi never produces atelectasis unless the bronchi are completely occluded. The severing of both phrenic nerves does not produce the lesion, nor is it found in many cases of paralysis of the diaphragm. An evident factor in the production of atelectasis which has not been considered, but which evidently is present, is fixation of the diaphragm. This factor we believe to have

been present in the case here reported. Keith<sup>1</sup> has called attention to the different factors concerned in the expansion of the upper and lower lobes of the lungs. The lower lobe is independent on the excursion of the diaphragm and lower intercostal muscles. The upper lobes are expanded by the action of the upper intercostals, the scaleni and the accessory muscles of respiration. It should be noted that paralysis of the diaphragm resulting from a lesion of the cord or from severing of the phrenic nerves does not prevent the ascent and descent of this

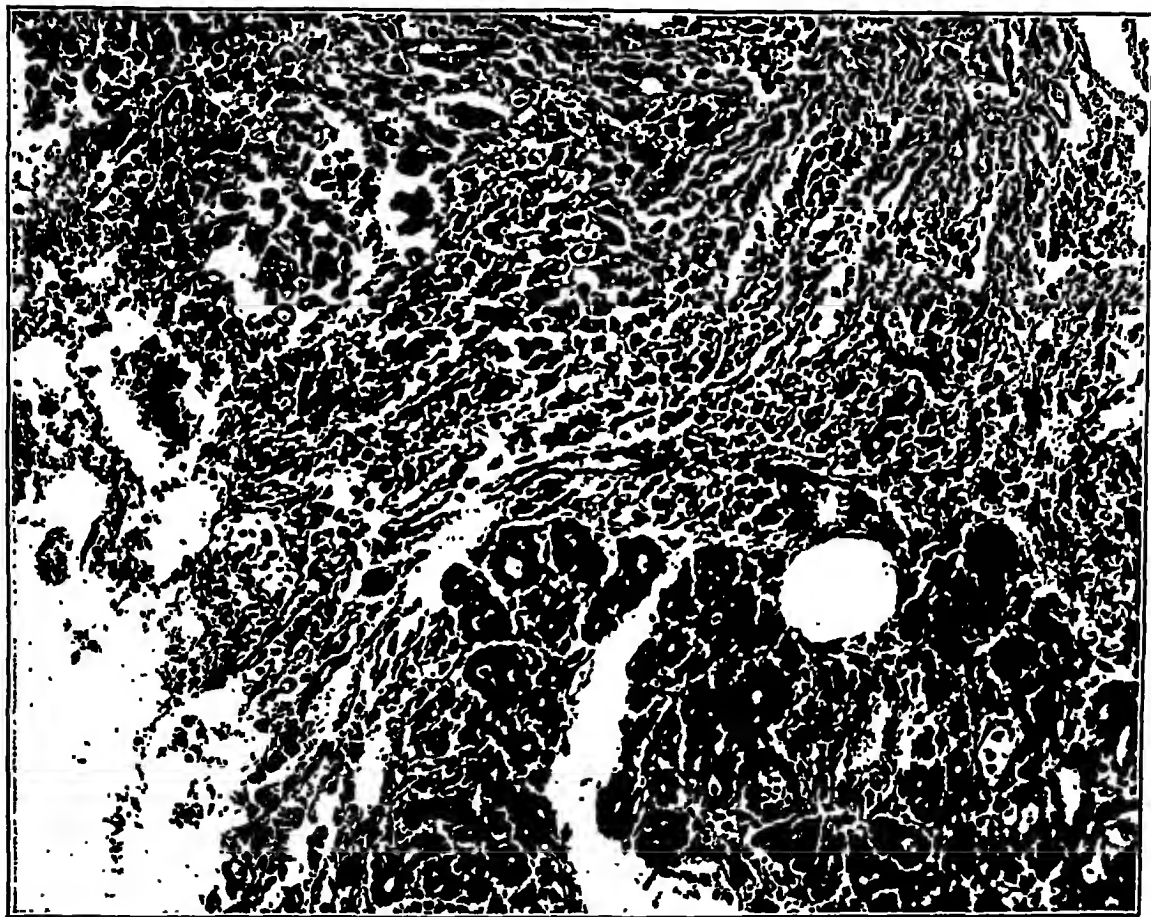


Fig. 8.—Acute pancreatitis—fat necrosis—, showing the presence of only a few parenchymatous cells;  $\times 160$ .

structure since it is then in a flaccid state and subject to intrapleural and intra-abdominal pressures. As in this case, fixation of the diaphragm evidently was present, the lesser peritoneal cavity was distended with fluid. Though the onset of the illness was evidently due to acute pancreatitis, three days later the patient had a transient cyanosis which is

1. Keith, cited by Soltau, A.: Massive Pulmonary Collapse. *Brit. M. J.* 1:544 (March 21) 1925.

typical of collapse of the lung. The roentgenogram taken five days after the acute onset of the illness shows what was probably a bilateral atelectasis of the lower lobes.

That the circulation continued through the atelectatic areas was well shown by the clean, glistening pleural surface and also by the well preserved structure of the interior of the lung. This of course would mean that a certain percentage of nonaerated blood returned to the left side of the heart. In the average patient, this deficient oxygenation of the blood would not be serious, but in cases of hyperthyroidism in which the oxygen consumption is greatly increased and also in cases of low cardiac reserve, this is a serious and sometimes a fatal complication.<sup>2</sup>

It is often stated in reports of cases of postoperative collapse of the lung that lobar pneumonia was a probable complication. In this case there was no pneumonic process and presumably the lungs in a patient of lowering resistance had been in a state of atelectasis for fourteen days. Impairment of the circulation in the atelectatic area was not sufficient to be evident.

#### SUMMARY

1. A case of bilateral lobar atelectasis in a woman, aged 48, is reported, the onset occurring three days after the onset of an acute pancreatitis (fat necrosis).

2. The observation that the lesser peritoneal cavity was distended with serum and the foramen of Winslow mechanically obstructed suggested the possibility that fixation of the diaphragm was the greatest factor in the production of a spontaneous collapse of the lower lobes of the lungs.

3. Collapse of either the upper or the lower lobe might be produced experimentally by removing all factors which are concerned in the production of the expansion of these lobes in the normal respiratory excursion.

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2. Ball, R. P.: Lobar Atelectasis Following Thyroidectomy and Lobectomy; Report of Four Cases with Necropsy Findings, to be published later in *Arch. Path.*

# SURGERY OF THE LUNG

## CARE OF THE STUMP IN PNEUMECTOMY AND IN LOBECTOMY \*

MINAS JOANNIDES, M.D.

Instructor in Surgery, University of Illinois College of Medicine

CHICAGO

Surgical treatment of the thorax is not a new field. Written records of thoracotomy in empyema and the recognition and drainage of pulmonary abscesses can be traced as far back as the time of Hippocrates in the fourth century B. C.<sup>1</sup> Hippocrates gave a detailed description of the course of pneumonia with the development of empyema and the steps of thoracotomy for the drainage of empyema. He recognized the development of pulmonary suppuration and regarded aspiration as the cause of it. After the time of Hippocrates, the subject was neglected until the beginning of the sixteenth century A. D., when Schenk, in 1584,<sup>2</sup> drew attention to this field. From that time on there were occasional reports of thoracotomies, and a great impetus was noticed with the introduction of methods of inducing artificial respiration by the Sauerbruch, the Brauer or the Meltzer technic. From this time on, thoracic surgery began its inception as a distinct specialty. In his brief but inclusive article, Willy Meyer<sup>3</sup> classified various operations on the lung that had been devised up to that time under four headings:

1. A single mass ligature around the bronchus and its vessels; amputation; cauterization of the mucosa of the stumps with pure phenol or the Paquelin cautery.
2. A single elastic mass ligature around the hilum and the removal of the lung at a second procedure ten days later (Lenhartz).
3. Ligature and division of the main bronchus with the remnant of the lung tissue stitched over the stump (Garré).
4. Isolation and temporary clamping of the bronchus; curetting of the bronchus; tight silk ligature; a second loose catgut ligature placed more centrally around the bronchus (Friedrich).

Meyer described a method for pneumectomy that he had found successful. The steps of his procedure are as follows: (1) isolation of

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\* From the Department of Surgery, University of Illinois College of Medicine and Rush Medical College, University of Chicago.

1. Hippocrates: E. Littré Edition, 1851. *Περὶ τοῦσιν τὸ δεύτερον*, vol. 7, chapter 44, p. 62, and vol. 7, chapter 57, p. 88; *Περὶ τῶν ἐντὸς παθῶν*, vol. 7, chapter 3, p. 174.

2. Schenk, quoted by Murphy, J. B.: *Surgery of the Lung*, J. A. M. A. **31**: 151 (July 23) 1898.

3. Meyer, Willy: *Pneumectomy with the Aid of Differential Air Pressure. An Experimental Study*, J. A. M. A. **53**:1978 (Dec. 11) 1909.



the bronchus, (2) clamping and crushing of the bronchus, (3) ligation and amputation and (4) burying of the stump and the use of top sutures. By using this technic, Meyer encountered only four deaths in twenty-one dogs on which total excisions of the lung were performed.

Other modes of handling the stump were developed from time to time. Thus, Halsted <sup>4</sup> performed twenty-one consecutive operations, and in only one was there primary infection of the pleura. He first isolated the bronchus; after bisecting it and removing the mucosa, he sutured the flattened edges together and held them with a series of sutures around the edges together with interrupted through and through sutures which encircled the cartilages.

Quinby and Morse <sup>5</sup> obviated the difficulty of pushing a large crushed portion of the main bronchus by treating each of the primary bronchi separately with the use of the technic employed by Willy Meyer.

Giertz <sup>6</sup> used a transplant of fascia lata to cover the crushed bronchial stump which was first sutured with silk mattress sutures.

Lilienthal <sup>7</sup> devised an ingenious technic for lobectomy. He applied a chain of pedicle suture ligatures and then excised the lung, leaving a generous stump. The ligatures were left long and were included in a rubber dam pocket, which prevented any of the remaining intrathoracic viscera from coming in actual contact with the stump. The rubber dam and the ligatures slough out and leave a healthy stump when they are removed.

It will be noticed that in practically all of the procedures mentioned little if any attention is paid to the vascular supply of the lung or the control of hemorrhage. I agree with Friedrich <sup>8</sup> that in surgical treatment of the lung hemostasis is the least troublesome factor, and that the success or failure of the operation depends on making a completely air tight stump. A few other factors must always be taken into consideration in operations on the lung. First, the lung expands and contracts with each respiratory movement so that the contiguous lobes interfere and make it necessary that they be packed away with wet gauze so that injury will not be produced. At times even a slight puncture with the needle or the tip of the knife causes an unnecessary amount of trouble-

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4. Halsted, W. S.: Clinical and Experimental Contribution to the Surgery of the Thorax, *Tr. Am. Surg. A.* **27**:119, 1909.

5. Quinby, W. C., and Morse, G. W.: *Experimental Pneumectomy: The Application of Data so Obtained to the Surgery of the Human Thorax.* Boston M. & S. J. **165**:121, 1911.

6. Giertz, K. H.: Ueber extirpation von Lungen und Lungenlappen mit Versorgung des Bronchial stump fes durch frei transplantierte Fascia lata, *Zentralbl. f. Chir.* **41**:1433, 1914.

7. Lilienthal, H.: *Thoracic Surgery*, Philadelphia, W. B. Saunders Company. 1926, vol. 2, pp. 147-169.

8. Freidrich, P. L.: *Thoracic Surgery*, J. A. M. A. **53**:1970 (Dec. 11) 1909.

some leakage of air and blood and makes it necessary to suture the lung by using either the Sauerbruch, Garré or a purse-string suture. Such an accident prolongs the operation and produces a greater tendency for shock and infection. Another important factor that aids in the success or failure of an operation on the lung is the length of time required. The quicker the operation is terminated, the better chance the subject has for recovery. By a mere thoracotomy the pressure relations of the intrathoracic and intra-abdominal organs are suddenly disturbed. In spite of the fact that intermittent positive pressure artificial respiration is maintained, and thus a stretching of the vessels of the lung provided for, as yet provision has not been made for the sudden increase of pressure exerted on the heart. Thus, the sudden and profound changes that occur in the circulation must be taken into account. I have often watched the heart become suddenly slow in rate and irregular in rhythm for no apparent reason, and only an injection of epinephrine or hydrochloride ephedrine would relieve this condition. In this case, if the heart is not stimulated promptly by means of an intracardiac injection of the drug, the animal either dies on the table or soon after the operation is performed. Another important factor that must always be considered is the sudden change in the temperature of the intrathoracic organs as a result of the thoracotomy. This sudden chilling undoubtedly has a definite injurious effect and must be prevented as much as possible. An important factor, indeed, is the manipulation and exposure of the virgin pleural cavity. The pleural surfaces are secretory and, like the peritoneal surfaces, any chemical, bacterial or mechanical irritation will produce an inflammatory change of a varying degree with subsequent exudation of serous fluid which has a tendency to change into a fibrinous and, later, a fibrous exudate, thus causing adhesions. The peritoneum has the same relation to the abdominal cavity as the pleura has to the thoracic cavity. It is inconceivable to think that a varying degree of pleuritis does not follow a thoracotomy. The most important consideration in surgical treatment of the lung is the upkeep of the process of oxidation in the body. I have found that dogs with an open pneumothorax do not live longer than ten minutes, at the most, after an intercostal opening of from 10 to 12 cm. Meltzer's insufflation anesthesia, which provides for a constant stream of air, is not satisfactory because it distends the lungs but does not make provision for contraction of the lungs. It is necessary that there be an intermittent blast of air so that an intermittent stretching and relaxing of the vessels of the lung may take place and thus the pulmonary circulation be kept up. In a series of experiments by means of which a sufficient amount of oxygen was supplied, a bilateral artery to vein transfusion being used, which was termed cross circulation, it was possible to double the length of life in the presence of an artificial pneumothorax. In these cases the lung stayed collapsed,



so that after the blood left the systemic circulation and entered the pulmonary circulation it encountered considerable resistance. As a result, a gradual engorgement in the lung of the recipient and a depletion of blood in the animal used as a donor were noticed. Thus, the donor died of an acute hemorrhage and the recipient of asphyxia and cardiac collapse. An intermittent artificial respiration obviates all this difficulty, because it not only supplies the lung with oxygenated air and provides for elimination of the carbon dioxide that is formed as a result of respiration, but it provides for the intermittent stretching and relaxing of the capillaries of the lungs that are so important in the welfare of the circulation of the blood.

Another factor of some importance is the disturbance to the vagus trunk of its branches as they enter the lung. In lobectomy, such as the Meyer type, one necessarily has to disturb the vagus. Under such conditions the heart, the circulation and the gastro-intestinal apparatus may be disturbed by the abnormal stimulation of the vagus. A factor recently was brought to my attention in some experimental lobectomies. In prolonged handling of the lung, an acute dilatation of the stomach, which proved fatal to the dog, was noticed. The difficulty was traced to a disturbance in the pillars of the diaphragm.<sup>9</sup> This disturbance may result indirectly through the lungs or directly through injury to the phrenic nerve or disturbance of the diaphragm itself.

With these facts in mind it becomes evident that one must find a method which will be simple and can be completed rapidly. It should control both the aeration and the vascular supply of the lung. It should provide for the avoidance of any unnecessary chilling or drying of the intrathoracic organs. I feel that the technic that is proposed here will satisfy the majority of these factors.

#### PROCEDURE

After a preliminary shaving of the dog and cleansing of the skin with soap and water, the skin is sterilized with tincture of iodine. The animal is now covered with sterile sheeting, and only the field of operation is left exposed. An incision is now made in the skin parallel to the ribs, and the platysma and latissimus dorsi are exposed. These muscles are incised in the direction of their fibers and are spread open so that the least amount of injury is caused to the muscles. These muscles are later utilized to cover the intercostal incision tightly. The intercostal space now comes into view. At this point I make sure that the epinephrine or ephedrine solution is ready for instant use. I also have the anesthetist get the apparatus for administering artificial respiration ready. The artificial respiration is now started, and a small nick is made down into the chest. As soon as the pleura is pierced, one can hear a wheezing. The incision is now enlarged by means of the finger or a blunt instrument. At this point artificial

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9. Hedblom, C. A., and Joannides, M.: The Relation of the Hiatus Esophageus to the Stomach. An Important Function of the Pillars of the Diaphragm, to be published.

respiration is stopped, so that the lung collapses, and in this way it is not torn when the intercostal incision is enlarged. This incision is usually made with the scissors. As soon as it is felt that a sufficiently large opening has been made in the chest, the artificial respiration is resumed and just enough pressure is exerted so that the lung expands and fills up the whole cavity of the chest.

The ribs are now spread apart with a self-retaining retractor, and the lung is pulled out by means of tissue forceps without teeth. At this point the artificial respiration is stopped again so as to allow the lung to collapse. Then a Kocher or Moynihan intestinal clamp with rubber tips is applied to the hilum (fig. 1). Just enough pressure is exerted with the clamp to stop the hemorrhage and control leakage of air when the lung is cut. Only a slight pressure is required for this clamping because the pressure in the lesser circulation is low, and the positive pressure in the artificial respiration apparatus is also low. Care must also be taken not to crush the tissues so that they will not slough. Artificial respiration is now started again and continued until the chest is closed.

Gauze moistened in hot saline solution is now used to protect the unexposed tissues and at the same time to catch any blood that will run out when the lung is cut. An attempt should be made to take out a wedge, and enough lung tissue must be left to cover over the stump (fig. 1). The lung should be cut at least 1 cm. distal to the compressing clamp. The bronchi are now isolated and ligated. The large vessels are also ligated. The suture is now started at the middle of the incision. This first suture is tied, but the end is left long so that it can be used later. A bite is now taken first on one and then on the other side of the first suture in such a way that the two sides of the wedge are brought in apposition. When the raw surfaces have all been covered with pleura, the compressing clamp is released and at the same time the suture is gently tightened. This maneuver accomplishes a double purpose. It allows the cut portions of the lung to become approximated more tightly, and at the same time it gives one an opportunity to look for leakage of air or blood. If the stump is airtight and watertight, the compressing clamp is removed and the chest is closed. If, on the other hand, the stump is leaky, the compressing clamp is retightened and additional interrupted sutures are used to cover the defect. The clamp is now removed, and the stump is left to drop back in the chest. Any blood that has found its way in the chest is now removed, and the chest is closed. In some experiments, the phrenic nerve is cut just before the chest is closed in order to produce a paralysis of the diaphragm and thus reduce that chance for suction through the stump. If the phrenic nerve is cut, care must be taken to ligate the pericardiophrenic artery, which is intimately attached to the nerve. In one case death was caused by hemorrhage from this vessel. Three fine wires are now used to aid in the approximation of the ribs. As they are inserted in the intercostal spaces with a number 1 or number 2 cutting needle, the underlying tissues are protected by means of a spatula which is placed on the parietal surface of the wall of the chest. In addition to the wire sutures, three interrupted heavy silk sutures are placed with the wires. The wires are pulled together, and thus the ribs are approximated. The silk sutures are tied and as soon as it is noticed that wheezing does not occur with each respiration, the artificial respiration is stopped. The overlapping muscles are now approximated and the wound is closed without drainage.

Care must be taken not to handle the heart or the pericardium any more than is necessary, because even the slightest handling has caused definite cardiac irregularity in the rhythm. The heart must be watched at all times and as soon as any slowing in the rate associated with cyanotic blood is noticed more air must

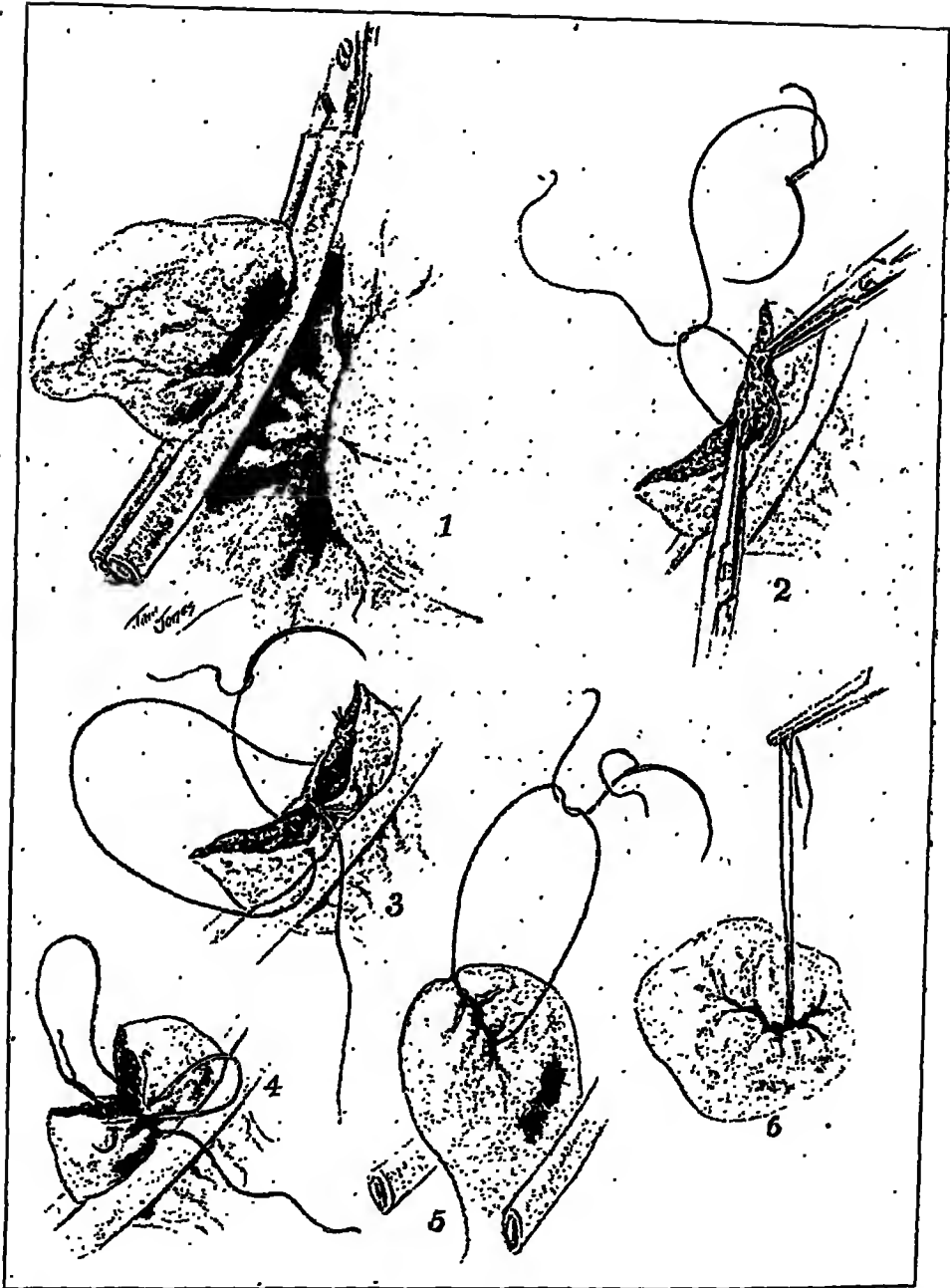


Fig. 1.—The important steps in the care of the stump. In 1, the arrow indicates the constricting clamp applied to the root of the lung; 5 shows the constricting clamp released and the suture tightened and 6, the appearance of the stump after the final knot is tied.

useful in the treatment of toxic abdominal distention, so-called. Bartlett,<sup>28</sup> too, found the employment of a dosage of 1/25 grain (0.002 Gm.) to give beneficial effects.

Cross<sup>29</sup> also advocated the use of the drug clinically combined with alternating doses of solution of pituitary, and at the same time gave experimental proof of his conviction by suspending a portion of the human appendix in Locke's solution and adding eserine and solution of pituitary, alternately. A stimulative effect is observed that is greatly

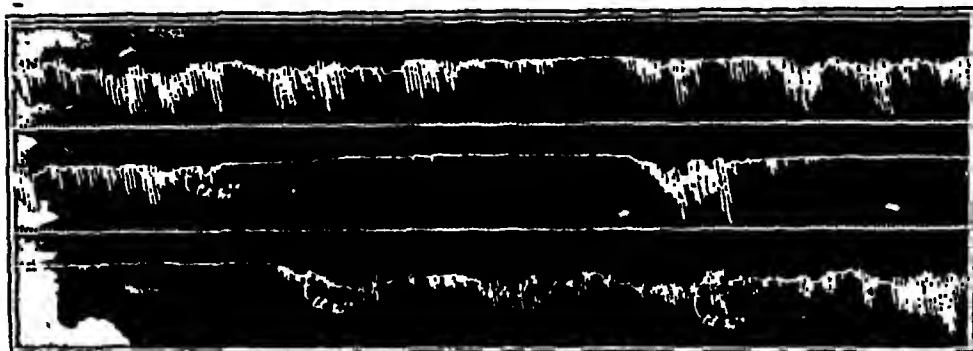


Fig. 5 (O. P. 34).—Record for dog obstructed for 165 hours. The top tracing shows a normal record; the second shows the effect of 0.025 cc. of pituitary fluid given intravenously. The third reveals that a repetition of the same dose does not produce any effect.



Fig. 6 (O. P. 36).—Record for dog obstructed for forty-eight hours. The normal tracing was for twenty minutes with maximum pressure of 32 cm. of water. The second tracing shows the effect of 0.5 cc. of oxytocin given intravenously, and the third of 0.4 cc. given intravenously twenty minutes later. The pressure was 5 cm. of water.

augmented by the addition of the second drug, no matter whether the eserine or the solution of pituitary is first employed.

28. Bartlett: *After-Treatment of Surgical Patients*, St. Louis, C. V. Mosby Company, 1918, p. 128.

29. Cross: *Brit. M. J.* 1:9, 1924.

# THE DEVELOPMENT OF BONE

- (A) THE PROCESS OF DEVELOPMENT IN BONES OF DIFFERENT TYPES;  
(B) NORMAL PHYSIOLOGIC CALCIFICATION OF THE MATRIX  
IN CARTILAGE AND IN BONE; (C) THE PROBLEM OF  
THE MANNER OF DEPOSITION OF THE  
CALCIUM SALTS

JAMES CRAWFORD WATT, M.D.

Associate Professor of Anatomy, University of Toronto  
TORONTO

In the studies here recounted, three different aspects of the problems involved in the development of bone are discussed, as indicated in the title. All three studies are closely interwoven and cannot be considered separately without much needless repetition and reduplication. Consideration is given each aspect in its proper relation to various portions of the work to be described, and they must be considered collectively for a proper elucidation of the problems discussed and for an interpretation of the results of the work which has been accomplished.

The process of the transport of calcium salts in the body and their deposition in bone have already been discussed in previous papers. But a much more thorough, detailed and minute study has now been made of the process of calcification of the cartilaginous and bony matrix of the skeleton, and the results obtained are embodied in this paper. It is to be remembered always that this calcification is a normal, physiologic process, and the conclusions arrived at by its study are far different from those derived from an examination of the pathologic process of calcification in various other tissues. A discussion of my views on the pathologic process is contained in a paper recently published,<sup>1</sup> showing that calcification in this case is a physical process of precipitation into dead or injured tissues and is not a function of the tissue cells. On the contrary, in the development and growth of the skeleton it will be shown that calcification is a function of the living cells and is dependent on their activity for its occurrence.

## MATERIAL

Bones in process of ossification were examined in their earliest stages by means of serial sections of young human embryos aged from 6 to 12 weeks. Formation of bone both in cartilage and in membrane was conveniently followed here, especially in the skull, without decalcifying.

Later stages were obtained by sectioning the humerus, radius, ulna, ribs and parietal bones from human fetuses of various ages from 4 to 9 months, and also

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1. Watt, J. C.: Deposition of Calcium Salts in Areas of Calcification, Arch. Surg. 15:89 (July) 1927.

The dose that we have administered was either 1/50 or 1/150 grain (0.001 or 0.0004), given for the most part intramuscularly. The only intravenous injections were made when 1/150 grain was used, all of which resulted in a definite increase in the intestinal motility except on one occasion when only a slight stimulative effect was noted. Following the intramuscular injections of 1/50 grain, there was a period of fifteen minutes, corresponding to the period of absorption, during which the intestines pursued their usual activity. A gradual rise in the intra-intestinal pressure then occurred, with subsequent abrupt increments, followed by a drop that was less in extent than the preceding rise until the pressure reached well above 100 cm. of water. This is much greater than is experienced in animals that have not been subjected to such stimulation, when it is rare to encounter a pressure greater than 50 cm. This period of increased intestinal motility continues for at least thirty minutes and may last an hour or even longer, though the usual duration is forty-five minutes. As

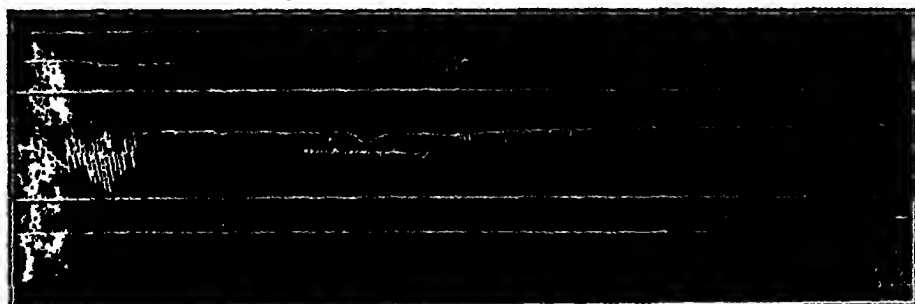


Fig. 7 (O. P. 36).—Record for dog obstructed for fifty-two hours. The normal motor activity is shown at the beginning of the second tracing when the pressure maximum is 30 cm. of water. After 0.25 cc. of vasopressin was injected intravenously there was little activity and none during the third tracing. The pressure was from 4 to 6 cm.

TABLE 2.—Effect of Eserine Sulphate on Intra-Intestinal Pressure During Obstruction of the Small Bowel

Dog		Drug	Quantity, Grain	Method of Injection	Maximal Intra-Intestinal Pressure, Cm. Water		Duration of Effect, Minutes
Serial Number	Hours Ob- structed				Before	After	
OP 27	25	Eserine	1/50	Intramuscularly	2-4	100+	25+
OP 27	31	Eserine	1/150	Intravenously	6	6-8	10
OP 27	31½	Eserine	1/150	Intravenously	6-8	28	10
OP 32	32	Eserine	1/150	Intramuscularly	6-8	42	15
OP 27	50	Eserine	1/150	Intravenously	10-12	100	30
OP 27	53	Eserine	1/50	Intramuscularly	8-10	93	40
OP 27	73	Eserine	1/50	Intramuscularly	2-5	105	30
OP 27	100	Eserine	1/50	Intramuscularly	10	80	40
OP 27	138	Eserine	1/50	Intramuscularly	6-8	114	15+
OP 28	25	Eserine	1/50	Intramuscularly	2-4	26	30
OP 29	22	Eserine	1/50	Intramuscularly	6-8	32	20+
OP 33	92	Eserine	1/50	Intramuscularly	44	60	50
OP 31	77	Eserine	1/50	Intramuscularly	6-8	68	70

similar specimens from young rats, some of which were new-born. For short and irregular shaped bones the tarsal bones of human fetuses aged from 6 to 9 months and those of children up to one month after birth were used, the navicular, cuboid, talus and calcaneus of one individual forming a set of four different stages valuable for comparisons. In these bones, ossification occurs as follows: the calcaneus in the sixth month, the talus in the seventh and the cuboid in the ninth month of intra-uterine life, and the navicular long after birth, usually in the fourth year.

#### TECHNIC

For the earliest stages small embryos were cut as a whole, while only the skulls of larger ones were used. For later stages, long bones were cut across the shaft so as to obtain about 5 mm. of bony shaft along with the cartilaginous epiphyses. Such a specimen was then split longitudinally and contained unaltered cartilage, calcified cartilage and newly formed bone in serial order in the section. Parietal bones were sectioned both transversely and tangentially. Tarsal bones were sectioned in their long axis, some of them serially.

All specimens were preserved in formaldehyde saline solutions and were sectioned without decalcifying so as to preserve calcium deposits intact. Duplicate specimens of some were decalcified to provide for ordinary histologic examination. All parts of the specimens remained intact on sectioning except for the hard, fully ossified shafts of long bones or the large ossified centers of some tarsal bones, which either broke somewhat or else slightly separated from the rest of the specimens at the line of junction with the calcified cartilage. Sections were cut 10 microns thick when possible, but when cutting was difficult they were made slightly thicker.

It is to be noted that there is a distinct difference in consistency between calcified cartilage and bone. Bone can be cut only with great difficulty, and only small areas of it can be gone through by the microtome knife without spoiling the sections and without danger of serious injury to the knife. Calcified cartilage is much softer and can be sectioned fairly easily.

In every case some sections were left unstained for both light and dark-field examinations, while other sections of each specimen were stained with hematoxylin and eosin and some with Mallory's triple stain.

#### I. PHYSIOLOGIC CALCIFICATION OF CARTILAGE PRECEDING OSSIFICATION

Preliminary to the occurrence of ossification in the skeleton there is a primary, rapid and transitory process of calcification in the cartilage about to be changed into bone. This process will be described in several different locations, and as it is best seen in the long bones formed in cartilage the conditions here will be first described.

*Calcification of Cartilage in Shaft of Long Bones.*—At the time when the budding blood vessels carrying osteoblasts with them invade the cartilaginous shaft of the future long bone in order to initiate ossification, the cartilage is seen to exhibit several well marked zones displaying different characteristics. These areas will be enumerated in order, passing toward the center of ossification.

At the extremities of the future bone (fig. 1, plate I), the cartilage cells are small and deeply stained and lie in a dense matrix which also

might be reasonably expected, the smaller doses have a correspondingly shorter period of effectivity. The figures followed by a plus sign in table 2 under the heading "Duration of Effect" do not represent the true period of action in all probability. At these times either another counteracting drug was injected, or the tracings and observations were discontinued.



Fig. 8.—Fresh longitudinal sections of dog's intestine cut from a normal animal under amytal anesthesia. The uppermost tracing shows the effect of 0.05, 0.2 and 5 cc. of pituitary fluid; the middle tracing shows the effect of 0.1 and 2 cc. and the lowest tracing shows the effect of 0.2 and 1 cc.



Fig. 9.—Effect of 0.5, 1 and 2 cc. of pituitary fluid in longitudinally suspended portions of a dog's intestine that had been obstructed 100 hours.

Corresponding to the solutions of pituitary there are also definite constitutional or general systemic responses. The chief of these is a twitching of peripheral skeletal muscle. This effect, in some instances, is violent. The other obvious physiologic responses were contraction of the pupil, salivation, slowing of the pulse and occasional vomiting. On two occasions pituitary fluid was given before the injection of eserine. In these instances, the muscle twitchings were much less and the intestinal motility not so violent and more normal in type.



stains well. Next to this lie zones in which the cells become progressively larger and more irregular in disposition and in which the staining of the matrix becomes paler.

Succeeding this, there is an area of transition terminating in the zone in which the enlarged cartilage cells lie close together in large lacunae arranged in columns. Between the cells of a column lie thin trabeculae of cartilage, while between contiguous columns lie heavy trabeculae of matrix. The cells of this area stain irregularly, and many appear to be degenerating and dying as the line of newly forming bone is approached. The matrix of this zone is heavily calcified and stains deeply with hematoxylin.

The final area seen in the specimen is one containing the primary marrow spaces with large blood vascular sinuses separated by trabeculae of calcified cartilage. On the latter, spicules of new bone are being deposited by the osteoblasts which were brought in with the blood vessels and now line the surface of the trabeculae.

On examining the calcium deposited in such a specimen as that described, one finds that in the bony spicules it is finely granular and requires fairly high magnification to reveal its nature. The cartilage trabeculae on which bone is being formed and the area of calcified cartilage immediately in advance of the line of ossification both exhibit a dense impregnation with calcium salts in the form of much coarser granules, which are all contained within the matrix. An interesting point in this connection is that around each lacuna there seems to be a thin layer of matrix which might be interpreted as the capsule for the cartilage cell, and this capsule does not contain visible calcium salts. The clear wall which is thus formed around each space is quite noticeable.

If stages previous to the occurrence of the center of ossification are examined, the processes which terminate in the calcification of the cartilage may be followed from their beginning. The earliest appearance of a change in the normal cartilage consists of two elements, first an increase in the size of the cartilage cells, and second, a matrix which becomes pale and no longer stains well.

Marking the next stage the cartilage cells arrange themselves in groups, and between contiguous groups the amount of matrix is fairly heavy and forms a substantial, branching, trabecular network. This matrix is darker again, staining fairly deeply, and indicates the areas which in later stages become most heavily calcified. These are destined to be the supporting trabecular network of calcified cartilage which is not eroded during the process of ossification but which remains as a sort of scaffolding on which newly forming bone is deposited in the ossifying area.

## HYPERTONIC SODIUM CHLORIDE

Among the first investigators to emphasize the value of sodium chloride in intestinal obstruction were Hartwell and Hoguet.<sup>30</sup> These workers found that the giving of physiologic sodium chloride solution to dogs with duodenal obstruction increased their life from a few days to about three weeks. In 1920, MacCallum and others<sup>31</sup> also noted that a large supply of chlorides prevented the symptoms of pyloric obstruction and restored the plasma chlorides to their proper level. Haden and Orr<sup>32</sup> were the first to investigate in detail the changes in the blood chemistry, which they found were most marked in high intestinal obstruction. To dogs they gave 50 cc. of a 10 per cent solution of sodium chloride with good results, but had animals live twenty-one and twenty-eight days when they gave 500 cc. of a 0.85 per cent solution daily. In one instance, the animal died soon after

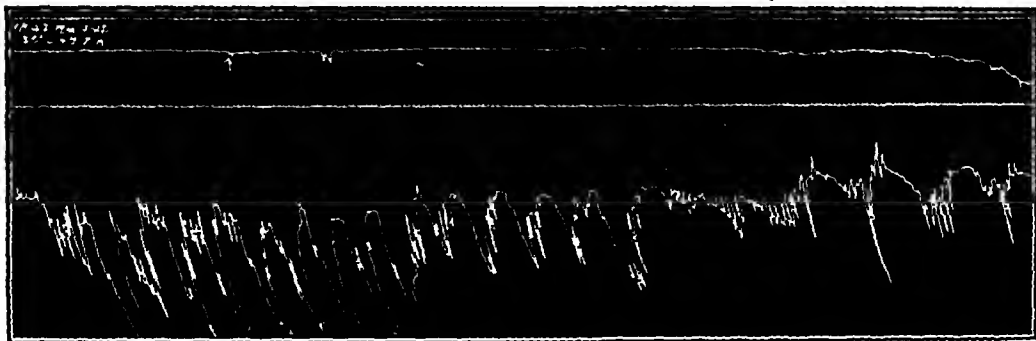


Fig. 10 (O. P. 27).—Record for dog obstructed for seventy-six hours. The arrow on the upper tracing shows the effect of  $\frac{1}{60}$  grain (0.0013 Gm.) of eserine sulphate given intramuscularly. Note the intestinal activity after fifteen minutes and still present at the end of the tracing, thirty-five minutes. The intra-intestinal pressure reached a maximum of 106 cm. of water.

an injection of a 25 per cent solution. Hughson and Scarff<sup>33</sup> were able to show experimentally that hypertonic salt solution not only prevents absorption from the intestine but also stimulates peristalsis, while its use in two clinical cases of paralytic ileus proved a great success after pituitary had failed completely. Ross,<sup>34</sup> also, both experi-

30. Hartwell, J. A., and Hoguet, J. P.: *Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution*, J. A. M. A. 59:82 (July 13) 1912.

31. MacCallum, Linty, Vermilego, Lyett and Boas: *Bull. Johns Hopkins Hosp.* 31:1, 1920.

32. Haden and Orr: *Bull. Johns Hopkins Hosp.* 24:26, 1923; *J. Exper. Med.* 38:55, 1923; *Surg. Gynec. Obst.* 37:465, 1923.

33. Hughson and Scarff: *Bull. Johns Hopkins Hosp.* 35:197, 1924.

34. Ross: *Canad. M. A. J.* 16:241, 1926.

## PLATE I

Fig. 1.—Longitudinal section of the phalanges of the finger of a seven months human fetus, showing developing bone in the shaft;  $\times 8$ .

Fig. 2.—Longitudinal section of the upper end of the humerus in a seven months human fetus. Note the numerous blood vessels in the cartilage forming the epiphysis, in which ossification does not commence until several months after birth;  $\times 8$ .

Fig. 3.—Longitudinal section of the elbow joint of a seven months human fetus. Blood vessels are numerous in the cartilaginous ends of the bones, which do not ossify until years after birth;  $\times 8$ .

All the illustrations are from photographs of specimens stained with hematoxylin and eosin except figure 10, in which the stain used was silver nitrate. The arrow, when used, points toward the center of the bone. In all the figures, *A.C.* indicates altered cartilage; *B.T.*, bone trabecula; *B.V.*, blood vessel; *C.C.*, cartilage cell; *C.C.T.*, calcified cartilage trabecula; *C.O.*, center of ossification; *G.D.*, granular deposit of calcium salts; *L.*, lacuna; *L.U.T.*, large, uncalcified trabecula; *L.W.*, lacunar wall free from granular deposit; *M.*, matrix; *P.*, periosteum; *P.M.C.*, primary marrow cavity; *S.T.*, stained trabecula and *U.C.*, unaltered cartilage.

mentally and clinically found hypertonic saline a great intestinal stimulant. Coleman,<sup>35</sup> in a review of his cases, found that the giving of 3 quarts of a 3 per cent solution reduced the mortality from 50 to 11.1 per cent.

In our studies we gave intravenously either 5 or 10 cc. of a 25 per cent solution. In all but one instance, we found a stimulative response. Generally, not only is there a rise in the intestinal tone, as is shown by an increase in the average rise of the intra-intestinal



Fig. 11 (O. P. 27).—Record for dog obstructed for 132 hours, showing the effect of  $\frac{1}{100}$  grain (0.0013 Gm.) of eserine sulphate given intramuscularly. The intra-intestinal pressure had reached 114 cm. of water when 1. cc. of pituitary fluid was given intravenously. Note the marked cessation of movement and the fall in pressure.



Fig. 12 (O. P. 34).—Record for dog obstructed for seventy-eight hours. The upper tracing shows a late effect (30 to 50 minutes) after 1 cc. of pituitary prepared by Park, Davis Company was injected. The lower tracing shows the effect of  $\frac{1}{100}$  grain (0.0013 Gm.) of eserine intramuscularly in the same dog fifteen minutes later. Note that the muscular activity is not so great as usually occurs after administration of eserine.

pressure, but the maximum levels are well above the normal. The duration of activity is generally about from twenty to thirty minutes. The motor activity is not so violent as after the administration of

35. Coleman, E. P.: Use of Hypertonic Saline Solution in Acute Intestinal Obstruction, J. A. M. A. 88:1060 (April 2) 1927.

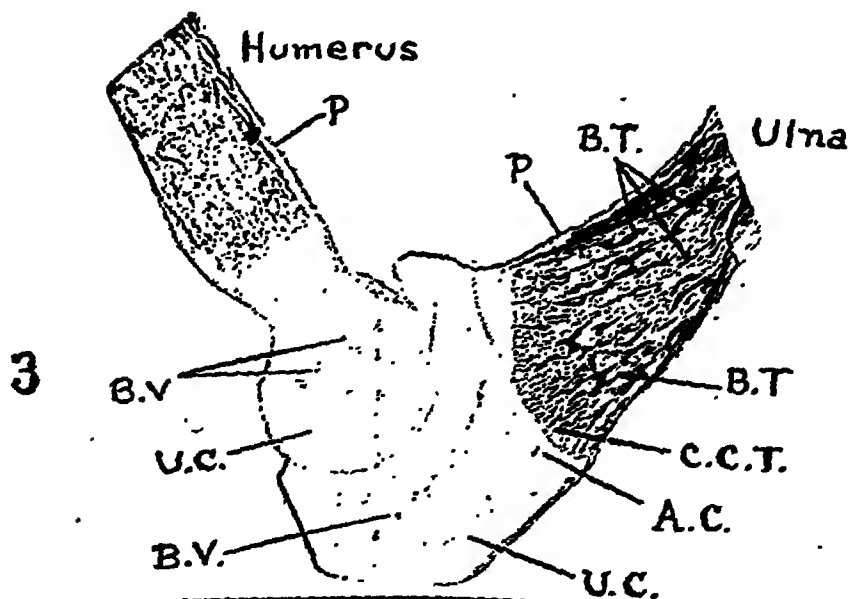
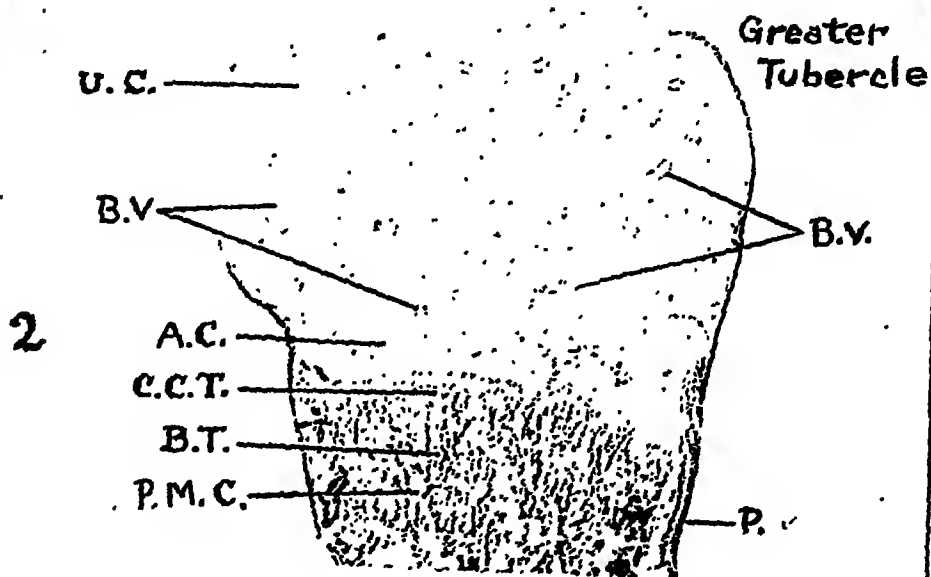
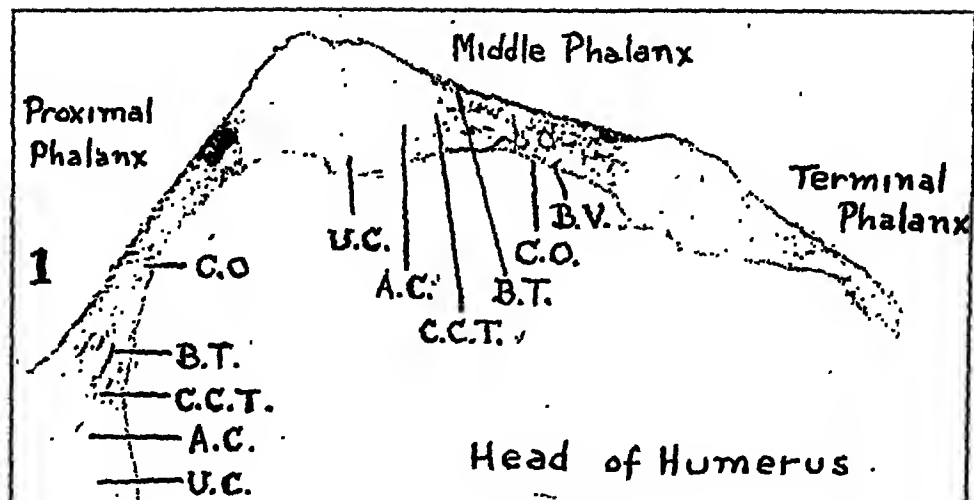


TABLE 3.—*Effect of Hypertonic Sodium Chloride on Intra-Intestinal Pressure During Obstruction of the Small Bowel*

Serial Number	Dog Hours Obstructed	Sodium Chloride, per Cent	Quantity, Cc.	Method of Injection	Maximal Intra-Intestinal Pressure, Cm. Water		Duration of Effect, Minutes
					Before	After	
OP 27	48	25	5	Intravenously	14-16	28	10
OP 27	49	25	5	Intravenously	6	18	20
OP 27	136	25	10	Intravenously	2-4	10	30
OP 28	7	25	10	Intravenously	2-4	2-4	..
OP 28	20	25	10	Intravenously	2-4	20	10
OP 29	22	25	10	Intravenously	2-4	32	20
OP 33	77	25	10	Intravenously	2-4	54	25
OP 33	96	25	10	Intravenously	30	36	30
OP 34	106	25	10	Intravenously	10	70	30
OP 34	187	25	10	Intravenously	5-6	58	25+

eserine, and the type of graph has the appearance of an increase in the normal rather than the changed character to the tracing obtained from eserine. In other words, the same rhythmic activity is found



Fig. 13 (O. P. 34).—Record for dog obstructed for 120 hours, showing the stimulative action of 10 cc. of 25 per cent sodium chloride intravenously. The intra-intestinal pressure rose to 57 cm. of water. The lower tracing shows the result of giving 1 cc. pituitary fluid.

after hypertonic saline is given as is found normally, except that the maximum change in pressure is greater than normal.

Ergotamine and pilocarpine were also given, and though each appeared to have a slight stimulative action, the extent of the response usually was not greater than the normal.

#### COMMENT

We have already enumerated the chief methods that are employed to investigate the intestinal motor response to various drugs, extracts and other therapeutic agents. In each it is easy to find when error is introduced, so that the employment of a new method, even though it does introduce new difficulties, is more or less justified so long as it overcomes some of the old pitfalls. And not only may it enable

Even before there is any visible deposit of calcium salts, the matrix of this trabecular network stains more deeply than the adjacent cartilage. The beginning of calcification in this region can be seen, and occurs as a deposition of small granules which appear first around the periphery of the lacunae of the cartilage cells. The thin layer of matrix forming the actual capsular wall of the lacunae is always clear of granules. The deposit increases and spreads in the matrix until the latter is completely filled with closely packed granules, which become almost a solid mass.

*Calcification of Cartilage in Epiphyses of Long Bones.*—The calcification of the cartilage of an epiphysis and its later ossification are initiated in the center of the mass. Before its appearance blood vessels are found in the epiphysis (figs. 2 and 3, plate I), invading it from various surfaces and branching within it so as to enclose a small central area within which are initiated all the changes terminating in its conversion into bone. Included among the vessels are some which penetrate the epiphyseal plate and enter the epiphysis from the end of the shaft of the bone. In all respects the epiphysis develops as though it were an independent bone, and the process is exactly similar to that found in the short, irregular bones such as the tarsals and carpals next described, so that the epiphyses should evidently be included in this next class.

*Calcification of Cartilage in Short, Irregular Bones.*—In the epiphyses of the long bones and in such bones as the carpals and the tarsals, there are some interesting differences from the process of development seen in the shaft of the long bone. The navicular, cuboid, talus and calcaneus of older fetuses and new-born children provide particularly good specimens for examination, giving all stages from solid, unchanged cartilage to complete calcification and the formation of true bone.

In these cases it was learned that blood vessels enter the cartilage and ramify in it for long periods, sometimes for many months (fig. 4, plate II), before the changes begin which accomplish ossification. In spite of their presence, the cartilage remains unchanged. The vessels enter from all surfaces except those articulating with other elements of the skeleton and penetrate to a zone about midway to the center, where they branch and run parallel to the surface, anastomosing freely. This vascular zone thus surrounds a solid central core of cartilage, the surface of which in contact with the vessels will be the exact external surface of the future calcified center of the developing bone.

Some time before the center of ossification is due to appear, changes occur in the cartilage preparatory in character to this event. There is first noticed a marked augmentation in the size of the cartilage cells in the region of the vessels and just proximal to them toward the center of the mass. Accompanying this change is a great increase in the amount of matrix between cells, and this matrix stains poorly and is pale.

us to get new ideas and conceptions about an old and long studied condition, but it may also serve to show how remedial agents affect that condition when their action is investigated in a new light. Therefore, the introduction of a new method of study, we feel, is justified in order that its efficacy may be tested and the results of previous studies confirmed or disproved.

In the main, this means of determining the action of various drugs on intestinal musculature does away with those difficulties that arise in the experiments on isolated muscles, such as temperature, acid-base equilibrium and nutritional factors. The drug that is added to the medium in which the isolated slip of muscle is suspended comes in contact with the muscle through a different path from that which approaches it through the blood stream. There is no interference with any of the local or general nervous mechanisms, while all those systems and structures such as blood pressure, through which a drug may exert its influence primarily or secondarily, are intact. In a moderate degree, too, a measure of the degree of the activity of a drug or extract may be gaged by its influence on the intra-intestinal pressure which is afforded a constant graphic representation. A repeated number of observations can also be made on the same animal. Of course, it must be borne in mind that each experiment is made on a dog that is in a pathologic state which each day becomes more severe, leading to a lowered resistance, gross changes in the blood chemistry and probable metabolic disturbances. These are comparable, however, to the same conditions that exist in human beings when the need for intestinal stimulants is paramount. So that the measures employed to prepare the animal for experimental purposes, and the early and late sequelae that result therefrom, do not introduce so great a degree of error as they would appear to do at first. A further point to be considered when comparing experiments on isolated tissue with those on the intact animal is that in the latter case the normal channels are present which influence the destruction or excretion of the drug.

A final interesting observation noted during these studies was the cause of death in one dog that was given repeated doses of eserine. While, for the most part, the animals would die from a complicating peritonitis resulting from a leak about the apparatus, in this dog, which received large and repeated doses of eserine that raised the intra-intestinal pressure greatly above what it would have been had this drug not been employed, the cause of death was from a perforation of the intestine. In this animal the small intestine was greatly distended for many inches above the site of obstruction; the antimesenteric border exhibited large diamond-shaped ecchymotic areas, ulceration of the mucous membrane and a fair sized perforation. A similar condition was not found in those animals to which eserine was not given. Indeed,



Immediately internal to the level of the blood vessels the cartilage cells now become irregularly grouped, not in columns as in the long bones but in clumps and small masses. Between these occur strips of matrix which do not contain cells, and which branch and intercommunicate and are destined to form the persisting cartilaginous network of trabeculae on which in later stages the first bone will be deposited. These trabecular areas give early indication of their future destiny (fig. 4, plate II; fig. 7, plate III, and fig. 10, plate IV) by staining more deeply than the remainder of the matrix and by being the first portion of the cartilage to become calcified. In later stages of development, it was quite noticeable that this intermediate trabecular zone adjacent to the blood vessels was completely calcified (figs. 5, 6 and 8), while the center of the mass still contained little if any calcium. Sections of a bone at this stage showed that there was a central region not yet calcified surrounded by a completely calcified layer; this again was surrounded by a ring of blood vessels and finally by a zone of unaltered cartilage on the exterior.

The first appearance of the deposition of calcium in these cartilages in every case was in the form of fine granules (fig. 11, plate IV) deeply stained with hematoxylin, lying in the matrix immediately outside the capsule of the cartilage cells, and always occurring first around those enlarged cells lying closest to the blood vessels. The primary zone of calcification is thus in the area of enlarged cartilage cells just internal or proximal to the blood vessels, and forms the calcified surface of a sphere (figs. 5 and 6, plate II), the center of which gradually calcifies later. This condition was extremely well shown in one talus which to the naked eye appeared completely calcified except for a thin external shell of unchanged cartilage, and which cut with some difficulty with the knife. In this specimen it was found, however, that cartilaginous trabeculae in the center of the area contained little if any calcium, although this was a later stage in calcification and the region was invaded by blood vessels and was full of primary marrow cavities, with beginning ossification of the area.

Blood vessels do not invade the central portion of the cartilage until it begins to calcify, but when once this process has taken place they erode and penetrate the periphery of the calcified mass (figs. 5 and 6, plate II) at various places and expand and anastomose within it, eroding large portions to form the primary marrow cavities. These are formed simultaneously with the occurrence of true ossification, which is now initiated with the deposition of bone by the osteoblasts on those calcified cartilaginous trabeculae which are not eroded. From this point onward, ossification advances toward the surface of the bone by growth on the

it is a rare occurrence in those dogs that die from simple intestinal obstruction to find at autopsy a perforation of the intestine at the antimesenteric border.

In discussing the results obtained from the use of pituitary fluid and pituitrin, we must admit that we found these different from what we had expected, though on more careful examination of the literature, not unlike those which other investigators had reported. When one observes in one place that solution of pituitary is a stimulant of smooth muscle and in another that it relaxes a suspended slip of small intestine, the only conclusion to be drawn is that either a different extract was employed in each case or the methods of observation introduced differences that in the end resulted in different conclusions. So far as the action of the extract on the isolated muscle is concerned, a great deal has been done to show the error that is introduced by depressor substances common to many tissue extracts, and also preservatives employed in the commercial products. Changes in the  $P_H$  of the bath as a cause of relaxation of strips of intestine have recently been emphasized by Gruber.<sup>36</sup>

The constancy of results that we have obtained, however, associated with the constant constitutional effects that have followed the giving of pituitary fluid, intramuscularly and intravenously, convinces us that they are true. Special precautions were taken to free the powder from which the fluid was made of all depressor substances, and a preservative was not added.

A word or two must be said about the change in the intra-intestinal pressure that is shown in table 1 under maximal pressures before and after injection. As a general rule, it is seen that the pressure in the column headed "Before" shows a greater pressure than that headed "After." The interpretation of this is that just before the injection of the pituitary fluid a period of increased intestinal pressure occurred, while after the injection the pressure fell off, and the intestine was apparently inactive until the effects of the extract had worn off. In some other instances, the pressure before the injection is not greater than after it. In these cases the intestine was apparently inactive for the few minutes immediately preceding the giving of the pituitary fluid, and no stimulation resulted with the exception of a continuation of inactivity and generally a falling off of the tone. Occasionally, a great degree of pressure is noted just before the injection. In these instances eserine had been given, and while it was still active, pituitary fluid was administered, which resulted in an abrupt fall of pressure.

So far as we could determine, there was no change in the degree of activity of the intestinal musculature following injections of pituitary

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36. Gruber: *J. Pharmacol. & Exper. Therap.* 30:73, 1926.

## PLATE II

Fig. 4.—Horizontal section of a cuboid in a seven months human fetus. This bone ossifies in the ninth month but already there is a pale central area surrounded by one containing a network of darkly stained trabeculae lying just within the zone of blood vessels;  $\times 8$ .

Figs. 5 and 6.—Sections of the talus (astragalus) of a seven months human fetus. The center of ossification occurs in this bone in the seventh month and is shown in the illustrations. It is really the center of calcification of the cartilage at this stage, and true ossification is just beginning to occur in it, coincident with its penetration by the blood vessels which are shown entering it;  $\times 8$ .

fluid so far as a relationship to the duration of the obstruction was concerned. The response in a dog in which obstruction for forty-eight hours was produced was the same as that in one obstructed six or seven days. In the same way, when a terminal peritonitis set in, a change in the usual response could not be observed.

The changes in the intra-intestinal pressure were observed for from one to two hours after the giving of the pituitary fluid. After from thirty to forty-five minutes, the changes in the pulse rate and the degree of pallor of the mucous membranes would have returned to normal. The rhythmic intestinal activity would also ensue in from twenty to forty minutes as a general rule, but a degree of activity or a rise in the intra-intestinal pressure that was greater than it had been before the administration of the pituitary fluid was never observed.

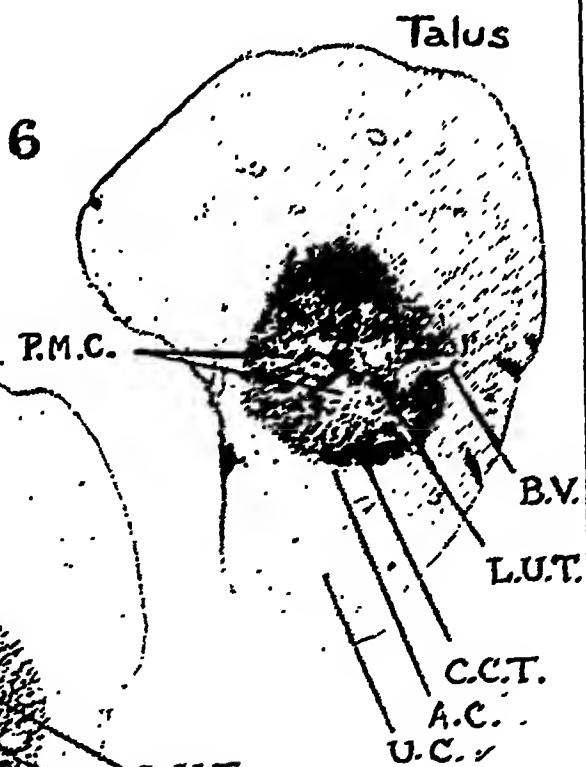
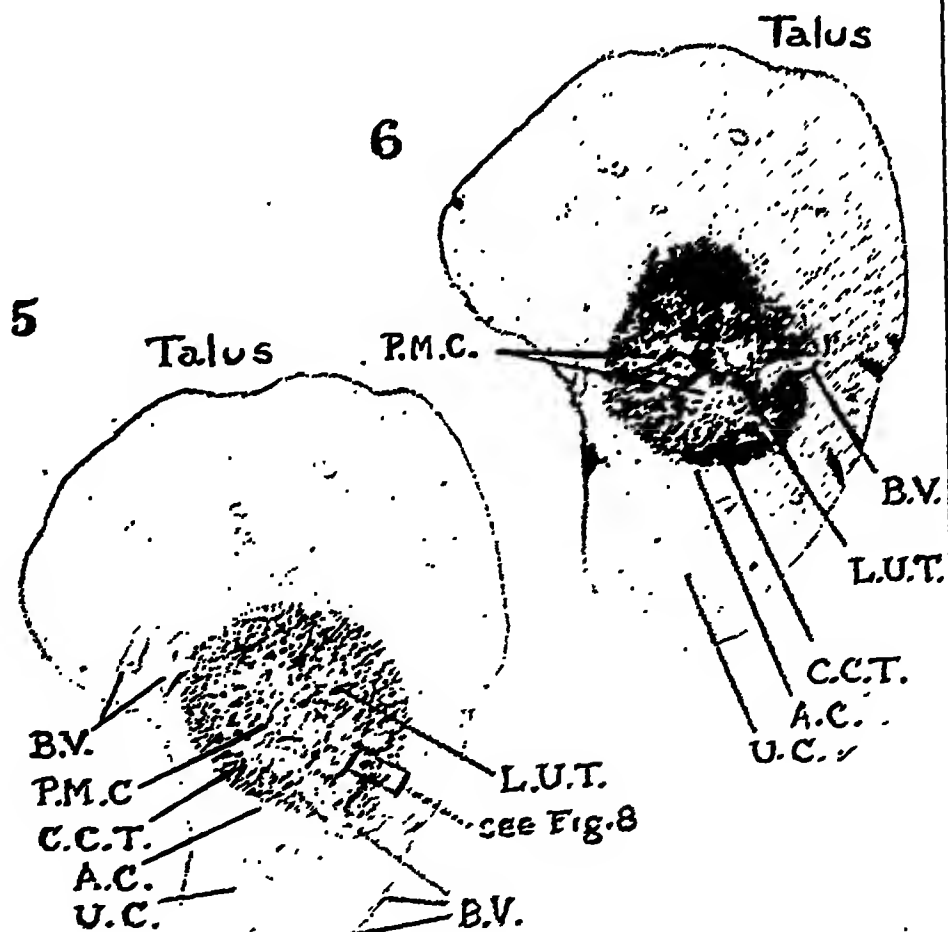
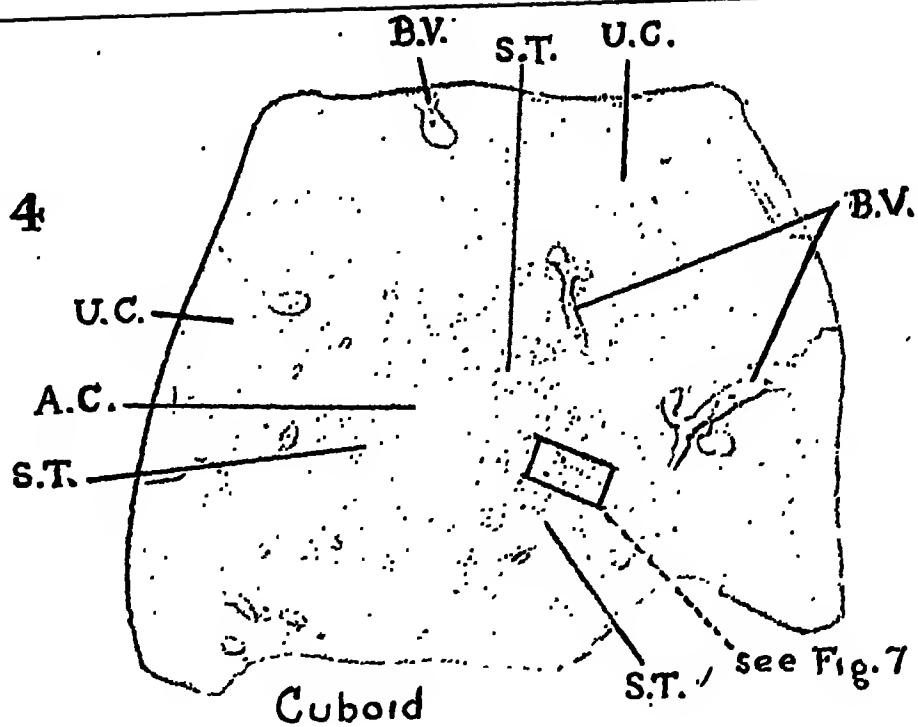
It must be stated that we have no record of the action of the solution of pituitary on the large bowel, nor have we any for the experiments on the isolated intestine. It is just possible that there might be a somewhat different response in this portion of the intestinal canal which would account for the defecation observed by some investigators following the injection of solution of pituitary.

An exact explanation of how this tissue fluid acts on the intestinal canal to bring about the results just stated is rather difficult. It would appear reasonable, however, to assume that, as the action of pituitary fluid on the isolated slip of intestine was no stimulation, a fall in tone or a cessation of rhythmic movements, while in the animal there was always a cessation of movement without exception, probably besides a possible direct action on the muscle itself; there was also a second factor, possibly the anemia of the wall of the bowel due to a vasoconstriction, or some other secondary effect.

While the use of pituitary solution is strongly advocated in all cases of intestinal paresis, it has by no means a constant and adequate therapeutic value. The opinion of various clinicians might vary so far as this point is concerned, but in the light of our studies, we should not expect a return of or an increase in the peristaltic activity following the use of the pituitary fluid we have employed.

In our experience, eserine was the most effective intestinal stimulant. Both in the response of isolated intestinal muscle to this drug and in all instances in which a sufficient dosage was given to the living animal, there was observed, as was previously stated, not only a rise in the tone of the bowel, but also a great increase in the degree of motor activity.

Hypertonic sodium chloride, too, would appear to increase the intestinal motor function. We are unable to state whether the extent of this action is greater when the blood chlorides have fallen to below normal, but we do feel that the stimulative power is greater late in the



obstruction. Reference should be made here to the work of Haden and Orr,<sup>37</sup> who stated that ligation of the dog's ileum at the ileocecal valve is followed by little increase in the nonprotein nitrogen of the blood, no change in the blood chlorides and carbon dioxide combining power of the plasma. This being the case, then, the value and efficacy of hypertonic sodium chloride as an intestinal stimulant would not bear any relation to the percentage composition of the chlorides in the blood.

#### SUMMARY

1. A method of recording the movements of the small intestine and the degree of intra-intestinal pressure in simple intestinal obstruction in dogs is described.

2. The effect of various solutions of pituitary and certain drugs on the movements of the small intestine and the intra-intestinal pressure in obstruction is recorded.

3. The action of pituitary fluid, pituitary, vasopressin and oxytocin on the obstructed intestine would appear to be one of depression and slight relaxation, though the general or other systemic effects induced by these extracts may vary considerably.

4. On the isolated portion of dog's intestine, whether from normal or obstructed bowel, the effects of pituitary fluid and pituitary are those of relaxation if any change occurs.

5. In the dog with intestinal obstruction, intramuscular injections of eserine in adequate amount have a decided stimulative action on the small intestine. The rise in the intra-intestinal pressure is also great and may measure more than 100 cm. of water.

6. The value of hypertonic sodium chloride as an activator of peristalsis is proved experimentally.

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37. Haden and Orr: *J. Exper. Med.* 37:365, 1923.

periphery of this central mass in the same way that it extends toward the ends of a long bone.

It will be seen that in all essential features calcification and ossification follow the same process in bones such as the tarsals as that followed in the long bones. The noticeable differences shown in the tarsal bones are: first, the early presence of blood vessels in the cartilage, long before the appearance of the centers of calcification and ossification; second, the appearance of calcium in the matrix at several places simultaneously to mark out a periphery for the region in which the alterations are occurring; third, the lateness of the occurrence of budding of the blood vessels and their formation of primary marrow cavities in the mass; fourth, the reversal of the direction of growth of the calcified area, which grows toward the entering blood vessels and not away from them as in the long bones.

*Calcification of Cartilage in Bones of the Skull.*—The development of the cartilage bones of the skull is similar in process to that in the rest of the skeleton and need not be described in detail. One point worthy of note, however, is the fact that calcification (fig. 9, plate III) may occur without any blood vessels being present in the cartilage.

In the skulls of young human embryos in which the cartilaginous rudiment of the future bones is not thick, it does not seem essential for their nutrition that blood vessels should be present in them. Preparatory to calcification, the matrix shows poor staining qualities and the cartilage cells enlarge as in other bones. The enlargement of the cartilage cells progresses until they are crowded one against another with a thin lattice or network of matrix between. At this stage, calcification of the matrix occurs by deposition of the calcium salts as granules in it. These granules are seen first immediately outside the circumference of the cells, and gradually those of contiguous cells merge to fill and make solid the partitions between adjacent cells. This obviously looks as though the placing of the granules was due to cellular activity.

Ossification follows this stage by the deposition of true bone subperiosteally on the calcified cartilage, and later this cartilaginous core to the future bone is gradually removed and replaced by true bone.

## II. PHYSIOLOGIC CALCIFICATION DURING OSSIFICATION.

Here two somewhat different conditions, due to the difference in origin of the bones developed in cartilage or in membrane, are considered.

*Ossification of Membrane Bones.*—In membrane bones the development was seen clearly in serial sections of the heads of young human embryos, the parietal bones and mandibles furnishing particularly good examples.

be given and also an intracardiac injection of 1 : 1,000 solution of epinephrine hydrochloride or 1 per cent solution of ephedrine must be administered. One cubic centimeter has been used with good results.

For artificial respiration, compressed air, which is forced into the lungs through a tin mask, has been used. The tubing is so arranged that either air alone or air saturated with ether can be given. If a varying degree and length of pressure on the floor of the mouth is applied in the dog, the amount and also the pressure of the air that is introduced into the lung can be regulated. The length and the degree of compression must be such that the lung distends to its full capacity in the open chest.

### RESULTS

Fifty-four partial or complete pneumectomies were performed on dogs. Nine of these animals died on the table during the earlier period of the experiments. As my associates and I became more expert in technic and as accidents and emergencies were watched for, the point was reached where the dogs survived the effects of the operation and lived for a long time. Of the nine that died on the table, six died of asphyxia caused by unsatisfactory artificial respiration. One dog died as a result of an accidental acute hemorrhage from the pulmonary artery. This hemorrhage resulted from the premature release of the compressing clamp at the hilum. The clamp could not be easily reapplied, and by the time it was reinserted the dog was exsanguinated. Digital pressure was not thought of until it was too late. Two other dogs died as a result of an acute dilatation of the stomach. This dilatation was encountered frequently, but two dogs were killed before it was found that a prompt emptying of the stomach with a tube was all that was needed. Another factor that shortened the postoperative life of the animals was distemper. Nine dogs developed this disease, and all died as a result.

All of the dogs showed evidences of pleural irritation with a greater or lesser amount of exudation. In those that died during the first ten days the chest was found full of serosanguineous exudate which would not clot either in or outside of the chest. Such a fluid was present on both sides. I believe that the fluid found its way into the opposite side through the thin mediastinum of the dog. Such has been my experience when fresh blood was injected into one side of the thorax. When the animal was killed two days later, the blood was present in about equal amounts on both sides. The site of suture was always found to be adherent to the wall of the chest and generally at the site of the thoracotomy. In the first ten days, the adhesions were fibrinous or a weak fibrous type. As the interval became longer the adhesions became stronger, so that in some cases the stump could be separated from the wall only by means of a sharp dissection (fig. 2).

Infection and leakage were encountered in one stump. In this experiment, an undue amount of strength was used to tie the suture and thus necrosis and a slough were caused.



During the first week the stump was dark purple and presented little crepitation. During this period, areas of hemorrhage into the interstitial tissue and the alveolar spaces were seen microscopically. At the site of the suture, the alveolar spaces were compressed in one direction and then were changed into strands of tissue (figs. 3 and 4). The bronchioles

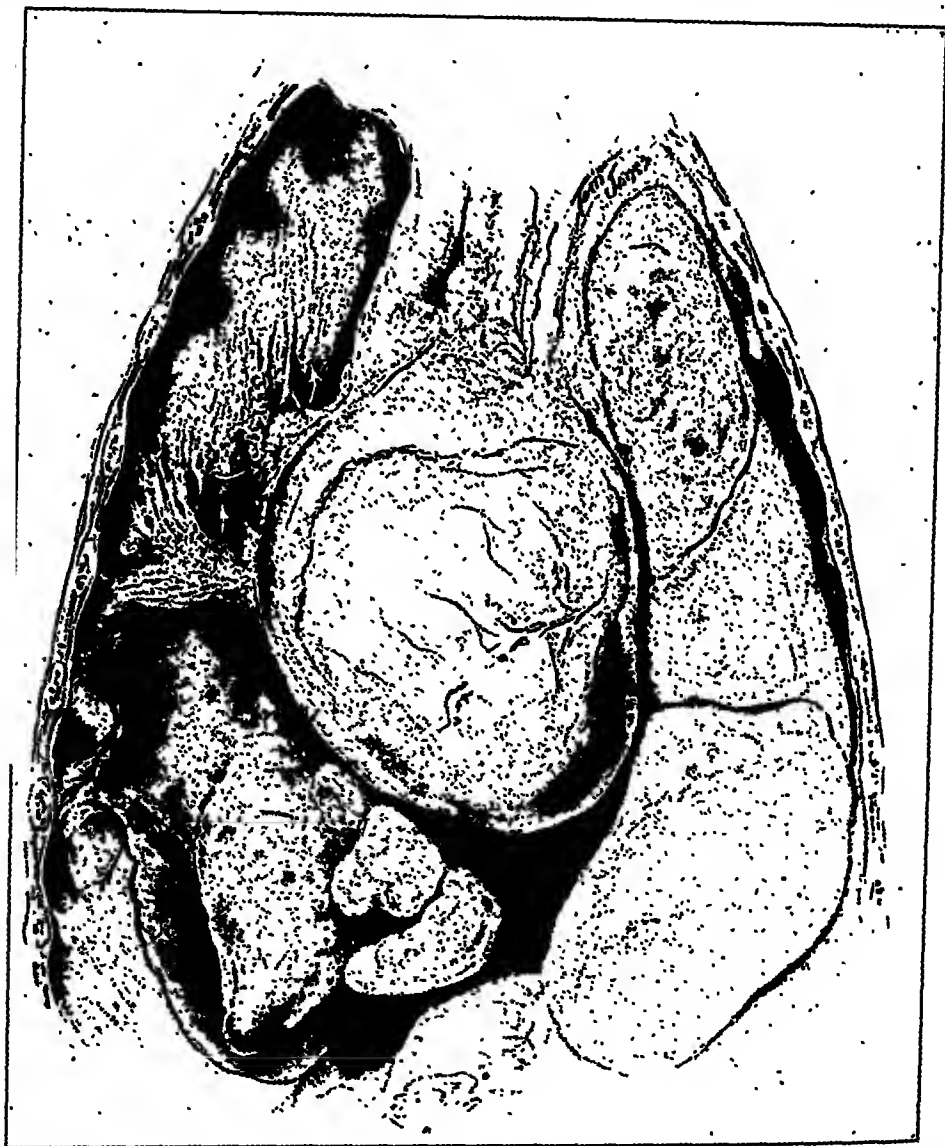


Fig. 2.—Appearance of the stump thirty-two days after an upper right lobectomy with the author's technic. The scar tissue binding the stump to the wall of the chest and pulling the mediastinum to the right side should be noted. The arrow points out the communications above and below the stump. Pathologic

The matrix of the osseous tissue is of a fibrous nature. In the fibrous membrane which precedes those bones developed in this manner, there is a ground substance which is already prepared for impregnation with calcium salts in a permanent form. The deposition of calcium salts starts on the surface of the membrane while it is still thin. Here a layer of cells under the sheath and in relation to a fairly good blood supply begins to impregnate the fibrous tissue on which they lie with a fine granular deposit. This occurs first in contact with the periphery of that side of the cell in relation to the membrane. As the cell becomes embedded deeper and deeper in the new bone which is being formed, the granules are found extending farther around the cell until finally it is entirely enclosed in a calcified matrix and is now a bone corpuscle as distinguished from an osteoblast. In stained sections, the granules form a dark border outlining the cells.

It is almost universally believed that the bone forming cells here exude the fibrous organic matrix, and from my studies I believe that the calcium salts are also exuded into this matrix or simultaneously with the matrix, where they then crystallize out or precipitate to give the bone its strength and hardness.

*Ossification of Bones Developed in Cartilage.*—In bones developed in cartilage, there is no matrix ready for permanent impregnation with calcium. The cartilage lying in any zone about to be ossified becomes calcified, but much of this is immediately removed by erosion and absorption. What remains is merely a temporary scaffolding to support the true bone which is first laid down on it and covers it. When the quantity of bone becomes sufficient for its own support, even this part of the cartilage is finally removed.

The bone which is first formed is deposited as a thin layer on the surface of the trabeculae formed of calcified cartilage. It is deposited by the secretory activity of the osteoblasts, which exude the organic matrix and simultaneously seem to pass the calcium salts into it. These salts first become visible in the matrix in an extremely fine granular form, the granules being much more minute than those seen in calcified cartilage. Whether the calcium salts become solid by a process of crystallization out of the solution or a process of precipitation is not known. I believe that their presence in the matrix is, however, due to the secretory function of the osteoblast in placing them in this position.

#### NORMAL CALCIFICATIONS

In the previous part of the paper, the facts as gleaned from my investigations of the development of the skeleton have been presented. It remains now to review these and to state the conclusions to which one may be led by them.

His conclusion is that faulty utilization of bone forming elements in rickets is due to defective absorption and that this in turn depends on a change in gastro-intestinal conditions.

Wilkins and Kramer<sup>13</sup> proved that the beneficial effect of cod liver oil on rickets could be obtained by an ether soluble extract injected intramuscularly, showing that the effect is a general one exerted through the circulation and not a local one simply due to the presence of the oil in the intestine. Flamini<sup>14</sup> showed that the antirachitic vitamin in cod liver oil increases the absorption of calcium from the intestine and aids in its fixation in the tissues.

In spite of their lower concentration in the blood of rachitic individuals the calcium salts are present in a supersaturated solution, according to Holt, La Mer and Chown,<sup>15</sup> and so the failure of the salts to be deposited in the bones must be due to more than a simple lack of precipitation.

Beckhold stated that precipitation of calcium is hindered by the colloids in the blood, and this hindrance must be prevented during ossification, the protective action of the colloids being changed at or by the bone cells. He also noted that Witte's peptone holds only calcium carbonate in solution, while calcium phosphate precipitates out of it. In this he saw the explanation of why there is so much more phosphate than carbonate in bone, because peptones are formed as the cartilage breaks down ahead of the ossification. In rickets there is an overgrowth of cartilage with less breaking down and, consequently, a smaller deposition of calcium salts and a softer bone.

Further evidence of the part played by the cell in the deposition of calcium in bone and cartilage is seen in the work of Robison, Kay, Soames and others.<sup>16</sup> They demonstrated that those tissues which utilize phosphates all possess a ferment called phosphatase, or esterase,

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13. Wilkins, L., and Kramer, B.: *Infantile Rickets: Treatment by Intramuscular Injection of a Cod Liver Oil Concentrate*, Bull. Johns Hopkins Hosp. 40:52, 1927.

14. Flamini, Mario: *The Action of the Antirachitic Vitamin of Cod Liver Oil on the Organism of the Child*, *Pediatrics* 34:625, 1926 (*Child Devel. Abstr.*).

15. Holt, L. E.; La Mer, V. K., and Chown, H. B.: *Studies in Calcification: I, II and III*, J. Biol. Chem. 64:509, 1925.

16. Robison, R.: *The Possible Significance of Hexosephosphoric Esters in Ossification: I*, *Biochem. J.* 17:286, 1923. Robison, R., and Soames, K. M.: *The Phosphoric Esterase of Ossifying Cartilage*, *Biochem. J.* 18:740, 1924. Kay, H. D., and Robison, R.: *The Action of the Bone Enzyme on the Organic Phosphorus Compounds in Blood*, *Biochem. J.* 18:755, 1924. Goodwin, H. W., and Robison, R.: *Phosphoric Esters of the Blood*, *Biochem. J.* 18:1161, 1924. Martland, M., and Robison, R.: *The Enzyme in the Early Stages of Bone Development*, *Biochem. J.* 18:1354, 1924. Robison, R., and Soames, K. M.: *A Chemical Study of Defective Ossification in Rachitic Animals*, *Biochem. J.* 19:153, 1925. Kay, H. D.: *Kidney Phosphatase*, *Biochem. J.* 20:791, 1926; *The Function of a Phosphatase in Bone Formation*, *Brit. J. Exper. Path.* 7:177, 1926.

## PLATE III

Fig. 7.—Photomicrograph of the area outlined on cuboid in figure 4. The arrow points to the center of the bone. Note the darkly staining trabeculae, although a visible deposit of calcium salts cannot be identified;  $\times 150$ .

Fig. 8.—Photomicrograph of the area outlined on talus in figure 5. The arrow points to the center of the bone. The cartilage cells are grouped in columns lying radially, and the dense black areas are the heavily calcified areas formed of closely packed granules. The granules are not visible in the photograph owing to the thickness of the section and the density of the stain taken by them;  $\times 150$ .

Fig. 9.—Photomicrograph of a portion of the base of the cranium of a human embryo 43 mm. long. The heavy black areas between cartilage cells in the center of the section are calcified areas densely stained. Blood vessels are not present in this cartilage;  $\times 150$ .

which will produce inorganic, ionizable phosphates from organic phosphoric esters. The phosphatase varies with the animal, the tissue and the age; it will stand considerable heat and can be kept for months and will still remain active.

Kidney phosphatase will hydrolyze all the acid-soluble phosphates in the blood, while bone phosphatase will hydrolyze only part of them. Bone phosphatase is not present before the beginning of ossification or in the cartilaginous ends; it is present in quantity in all bone, even in old age and is in maximum amount in the ossifying zones during growth and is coincident with and in proportion to the amount and rapidity of growth.

Eden<sup>17</sup> found large amounts of calcium in the callus of healing fractures, which were transparent on roentgenographic examination. The calcium was evident here in a form bound to the protein of the callus. He also made injections of solutions of calcium salts into the site of fracture and obtained much more rapid healing, showing the effect of a good supply of calcium on cellular activity.

Rabl<sup>2</sup> said that the calcium in growing bones is to be found in a form bound to peptids and amino-acids formed by the breaking down of the cartilage in the region. Carbonates are produced through the liberation of carbon dioxide on further decomposition and the phosphates precipitate by reaction with soluble phosphates of the tissue fluids. One might see here the use of the esterase previously mentioned in increasing the amount of available phosphates.

The problem raised here does not yet appear capable of solution, but consideration of the facts leads to the assumption that the cell must have considerable influence on the deposition of calcium salts in cartilage. The weight of evidence, one feels, is in favor of the view that the cartilage cell has some secretory activity, the exact process of which is as yet unknown, which is accountable for placing the calcium in the matrix.

This view is similar to the one I have already advanced that the calcium contained in the matrix of the bone is deposited by secretory activity of the osteoblasts and bone corpuscles, and my reasons for inclining to this view have been fully set forth in previous papers.<sup>18</sup>

The deposition of calcium in bones developed in membrane, being in the form of fine granules immediately surrounding the osteoblasts

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17. Eden, R.: Untersuchungen über Vorgänge bei der Verknöcherung, *Klin. Wchnschr.* 2:1798, 1923.

18. Watt, J. C.: The Behaviour of Calcium Phosphate and Calcium Carbonate (Bone Salts) Precipitated in Various Media, with Applications to Bone Formation, *Biol. Bull.* 44:280 (June) 1923; The Deposition of Calcium Phosphate and Calcium Carbonate in Bone and in Areas of Calcification, *Arch. Surg.* 10:983 (May) 1925; The Transport and Deposition of Calcium Salts in the Body, *M. J. Australia* 2:85 (July) 1925.



PLATE III

(which also form the bone corpuscles when fully embedded), is in all essentials similar to the process of calcification of cartilage, and its consideration leads to similar conclusions.

It is interesting to note in this regard that Weidenreich<sup>19</sup> published two comprehensive articles on the constitution of bone, in which he described three divisions of this tissue: fiber bone, cartilage bone and lamellar bone. He considered the lamellar bone of the haversian systems as being the only true organized bone tissue, with true bone corpuscles and with a finely granular calcium content to its matrix, which may be even homogeneous from fusion of the deposits into a mass.

Fiber bone is regarded as simply a dense calcification of fibrous tissue; it is found as the subperiosteal deposit on the surface of all bones, in muscular prominences of the skeleton and in all the bones formed in membrane. It can also be seen in ossified tendons. The deposit of calcium here is in a much coarser granular form.

Cartilage bone is seen in the early embryonic ossifications and also in the calcification of certain epiphyses, especially those occurring late, and contains calcium in a coarse granular form.

The two latter forms of bone appear in the embryo and also during later growth as the kind of bone which is formed first in any location. Much of this material is later reorganized and converted into the lamellar type by activity within the bone. What I have found true, especially concerning the physical state of the calcium salts in various bones, is in perfect accord with Weidenreich's statement.

Two other instances of normal calcification which may be considered are the formation of the shell in the hen's egg and the shell of the fresh water clam. Both of these structures are regarded as products of secretion. The clam shell is considered due to the secretion of calcium carbonate in albumin on the surface of the animal's mantle. This salt, as Pauli and Samec<sup>20</sup> showed, is seven times as soluble in albumin as in water and so can be secreted in appreciable quantity. The solubility is also increased by the carbon dioxide content of the tissues. When the secretion is exuded on the surface of the mantle, the lowered carbon dioxide content of the water causes the calcium carbonate to precipitate. Being in a colloidal solution it separates out in the colloidal form of deposit, which is usually small spherules; these have a marked

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19. Weidenreich, F.: Knochenstudien: I. Ueber Aufbau und Entwicklung des Knochens und den Character des Knochengewebes. II. Ueber Sehnenverknöcherungen und Faktoren der Knochenbildung, *Ztschr. f. Anat. u. Entwicklungsgeschichte*, 69:382 and 558, 1923; Ueber den Begriff "Knochen" und die Beziehungen des Knochengewebes zu Bindegewebe und Knorpel, *Anat. Anz.* 57:138, 1923.

20. Pauli, W., and Samec, M.: Ueber Löslichkeitsbeeinflussung von Electrolyten durch Eiweisskörper, *Biochem. Ztschr.* 17:235, 1909.

In the case of those bones which are preformed in cartilage, it may be stated that calcification of the cartilage occurs in all cases previous to ossification. The calcified cartilage is not transformed directly into bone but is removed. Much of it is immediately absorbed, while the remainder, forming a scaffolding of trabeculae for the support of the bone which is first produced, is later absorbed, when the true bone is formed in sufficient amount to support the skeleton.

The cartilage may go through all the changes ending in calcification, without the presence of any blood vessels (fig. 9, plate III) in it if it is small or thin, as may be seen in the case of some bones of the skull. But if the cartilage is of larger mass (fig. 2, plate I and fig. 4, plate II), then blood vessels will be present in it. However, they will stop just short of, and will not ramify in the calcified area itself until that moment (figs. 5 and 6, plate II) when the area is invaded by the budding blood vessels carrying in the osteoblasts to initiate true ossification.

An interesting view has been suggested to me to explain the presence of a skeleton formed of calcified cartilage in the embryo. It will be recalled that in the lowest forms among the vertebrates the skeleton is not true bone but is only a calcified cartilage. The bony skeleton first appears in the higher fishes, replacing a cartilaginous one. Thus the temporary appearance of a calcified cartilaginous skeleton for a short time just previous to the appearance of the permanent bony skeleton in the embryo of all higher vertebrates is to be interpreted as an evolutionary phenomenon, reflecting the past history of the race. It is a case of phylogeny being repeated in ontogeny in the skeleton in a way similar to that seen in the case of the kidney. In the latter, there is the succession of pronephros, mesonephros and metanephros as excretory organs, only the last persisting as a kidney in the highest vertebrates. In the skeleton one finds the succession of cartilage, then calcified cartilage and finally bone.

The calcifying of the cartilage, which is thus so temporary and transient, appears to serve a practical purpose in the embryo by providing a large amount of calcium ready for use by the osteoblasts in the first rapid formation of bone.

In those bones developed in membrane, the organic matrix necessary to receive the calcium salts is already present and does not need to be altered, as was the case with the cartilage, so the more permanent deposition of salts is made directly into this fibrous matrix. The latter is similar to the new matrix that is formed by the osteoblasts which produce bone in a cartilaginous area. The method of bone formation in membrane is therefore much like a calcification of fibrous tissue, with this difference, however, that the calcium salts appear in intimate relation with the characteristic tissue cells, namely, the osteoblasts and bone



tendency to fuse and so produce the dense pearl shell. The contact of the water with the albuminous solution no doubt aids in the precipitation also by its tendency to dilute the albumin and so render the contained calcium salt less soluble.

The process of formation of the clam shell is thus seen to be a double process. There first occurs secretion of the calcium carbonate in a soluble form in an albuminous matrix through the agency of the mantle cells. Secondly, there is a precipitation and fixation of this secretion by physical and chemical means, through which the calcium carbonate combined with the albumin in colloidal crystals is deposited. That albumin combines with the crystals was shown previously as far back as Rainey's<sup>21</sup> period by decalcifying experimental precipitates and obtaining perfect albuminous casts of the deposits after the calcium is removed.

A second example of the secretion of calcium is to be found in the formation of the shell of a bird's egg. The shell is composed almost entirely of calcium salts and is secreted by the shell gland, a modified part of the genital tract, and an evident and undeniable cellular activity is concerned here in the output of calcium. The final deposition in solid form about the egg may again be a precipitation due to the concentration of carbon dioxide found in the genital passage which is lower than the concentration existing in the tissues. But the placing of the calcium here where it can precipitate is certainly due to the secretory work of the mucosa of the shell gland in taking the calcium salts from the blood stream and passing them through to its free surface.

In the case of the formation of the teeth, the manner in which calcium is deposited again comes into question. There is a definite organic matrix to both the enamel and the dentine, laid down, respectively, by the ameloblasts and the odontoblasts.

In the matrix of each layer, the calcium is found deposited in the form of minute granules. These were interpreted by Rainey, and by others since his time, as indicating their production by precipitation, as they are exactly of the form and appearance seen in experimental precipitation of calcium carbonate in colloids. But the inorganic material of the teeth is largely calcium phosphate, which has been shown (Rainey,

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21. Rainey, G.: On the Formation of the Skeletons of Animals, and Other Hard Structures Formed in Connection with Living Tissues, *Brit. & Foreign Med. Chir. Rev.* 40:343, 1857; Precise Directions for Making of Artificial Calculi with Some Observations on Molecular Coalescence, *Quart. J. Micr. Sc.* 6:41, 1858; On the Structure and Mode of Formation of the Dental Tissues, According to the Principle of Molecular Coalescence, *Quart. J. Micr. Sc.* 7:212, 1859; Some Further Experiments and Observations on the Mode of Formation and Coalescence of Carbonate of Lime Globules, and the Development of Shell Tissues, *Quart. J. Micr. Sc.* 1:23, 1861.

corpuscles. The development of bone in membrane is, of course, also phylogenetically significant, for it, too, repeats the history of development of this type of bone.

In all cases of calcification of cartilage observed, the following facts are to be noted:

1. The calcium salts always appear first in the form of granules.
2. These granules appear first around the cartilage cell (fig. 11, plate IV) and are embedded in the matrix immediately outside of the cell capsule.
3. The salts appear before blood vessels are present in the calcified areas.
4. The calcium salts do not appear until after changes have occurred both in the cartilage cells (fig. 4, plate II; fig. 7, plate III, and fig. 10, plate IV) and in the matrix of the area to be calcified. The cells become grouped and greatly enlarged; the matrix increases considerably, becomes pale and stains poorly.

It thus appears that the association of calcium deposits with the cartilage cells is close and that the whole manner in which calcification occurs leads to the conclusion that the cell has considerable control of it, and that the calcium arrives in the matrix somehow as a result of the cell's activity.

According to all investigators, precipitation of calcium salts in solution in the body tissues occurs when the carbon dioxide content is lowered. It seems reasonable to infer that the matrix farthest away from the cells in the cartilage would contain the least carbon dioxide which, being a product of the activities of the cells, should be most concentrated in its immediate neighborhood. If this inference is correct, the first place in which calcium salts would be deposited would be in the larger masses of matrix and as remote as possible from surrounding cells. This is not the case, but the opposite is true. The first deposition is immediately surrounding the cell capsule, so that the granules evidently do not occur by precipitation from decrease of carbon dioxide in the cartilage.

The view has been put forth that calcium salts are precipitated as carbonate and phosphate by the reaction of these radicles excreted by the cells uniting with calcium dissolved in the fluids of the matrix. If this were so, one would expect the deposition to be equal all about the circumference of the cell, but in the early stages of calcification the deposit is frequently found lying all to one side of the cartilage cell, although there was plenty of opportunity for it to be surrounded completely.

Harting,<sup>22</sup> Watt) to precipitate even in colloids as an extremely fine granular suspension. Only the carbonate forms globules and spherules, so that the constant appearance of the calcium phosphate in the teeth in globular form is not to be interpreted without question as indicating a simple precipitation.

The problem as to how the calcium actually deposits in the enamel or the dentine of a tooth is underlaid by a still more fundamental problem as to how the calcium salts are brought into this region where they are later laid down. If they simply diffuse into the matrix, then the whole process of deposition is a simple precipitation. But if they are selected and passed into the region by cellular activity and then appear as a solid deposit, it is evident that although the end of the process may still be a precipitation, nevertheless, the beginning is a vital process, secretion by the cells forming this tissue. This is an important and far reaching difference and is of great significance in understanding the development of the teeth; it will modify radically all attempts to treat abnormal conditions such as defective calcification.

Concerning the teeth, Blotevogel<sup>23</sup> did work which is of great significance. He made injections of trypan blue into young mice and then examined the developing teeth at intervals of from one to thirty days. He found that the ameloblasts, which form the enamel, and the odontoblasts, which produce the dentine, both stored the vital dye evenly throughout the cell before they became active. But when they began to form the enamel and dentine, both these types of cells showed marked polarity, with a definite direction of transport of material through the cell. This was shown by the fact that all granules became closely packed along that edge of the cell which was forming the enamel or the dentine. The organic matrix of the enamel or dentine formed during the period when the dye was present was also colored diffusely blue.

When the enamel and dentine became calcified the parts which contained calcium were colorless, either because the calcium does not combine with the dye or because it bleaches it. This is the opposite effect to that seen with madder or alizarin, which combines with calcium, as shown by Macklin,<sup>24</sup> and is deposited with it as a colored compound if the dye is present at the time of deposition.

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22. Harting: On the Artificial Production of Some of the Principal Organic Calcareous Formations, *Quart. J. Micr. Sc.* 12:118, 1872.

23. Blotevogel, Wilhelm: Beiträge zur Kenntnis der Stoffwanderungen bei wachsenden Organismen: II. Der vitale Farbstofftransport während der Zahnentwicklung, *Ztschr. f. Zellen-u. Gewebelehre* 1:601, 1924.

24. Macklin, C. C.: Studies in Calcification by the Use of Vital Dyes, *J. M. Research* 31:493, 1917.

## PLATE IV

Fig. 10.—Photomicrograph of a section through a cuboid slightly further advanced than that shown in figures 4 and 7. The cartilage cells are in irregular groups with darkly staining heavy trabeculae between them, which will become calcified and form the scaffolding for the future deposit of bone;  $\times 150$ .

Fig. 11.—Photomicrograph with high magnification of the area in a cuboid which is just beginning to calcify. The cells lie closely packed in irregular groups and in the matrix between them can be seen the black, densely stained masses of calcium deposit which in favorable places, when not too heavy, can be seen to be composed of closely packed granules. In those lacunae which are sharply in focus the actual lacunar wall is seen to be free from granules;  $\times 500$ .

Blotevogel found conditions in bone similar to those in dentine, uncalcified matrix colored with trypan blue and calcified areas unstained. The osteoblasts, forming matrix on all sides of them, stored the blue evenly in contrast to the odontoblasts which, forming dentine only on one side, stored all the blue at that side. A definite direction of transport of material and an evident cellular activity in handling this material has been beautifully demonstrated here. It may be inferred that what can be done in the case of trypan blue could be done also in the transport of calcium salts. A definite cellular activity can be demonstrated in the formation of the organic matrix of tooth, bone and cartilage, and the evidence all seems to point to the occurrence of a similar process in the impregnation of this matrix with the calcium salts.

Further collateral evidences that cellular activity is responsible for the handling of calcium in bone and cartilage may be cited. In Vincent's<sup>25</sup> book on "Internal Secretions and the Ductless Glands" are many instances, given with reference to original papers, of the influence of hormones on the growth of bone. The changes in acromegaly, the increased stature in eunuchs, the increased growth of bone in cretins treated with thyroid extract and other instances all go to show the effects of hormones.

Hammet<sup>26</sup> showed that thyroid and parathyroid deficiencies produce marked changes in the bones, especially in proportions of water, organic matter and bone salts. Parathyroidectomy lowers the calcium and phosphorus content and increases the amount of magnesium. This author also showed that all bones are not equally sensitive to disturbances in hormone control, the humerus, for example, being less resistant than the femur.

Rachitic changes in the bones of rabbits and rats the thyroid glands of which were removed three weeks after birth were demonstrated by Kunde and Williams<sup>27</sup> in spite of the administration of adequate diets to the animals.

Fahr<sup>28</sup> described marked changes of the endocrine system in the case of osteogenesis imperfecta and expressed the belief that these

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25. Vincent, S.: *Internal Secretions and the Ductless Glands*, Toronto, The McMillan Company, 1912.

26. Hammet, F. S.: *Studies of the Thyroid Apparatus: XLII. The Role of the Thyroid and Parathyroid Glands in the Growth of the Long Bones*, *J. Exper. Zool.* **47**:95, 1927; *XLIII. The Role of the Thyroid and Parathyroid Glands in the Growth of the Long Bones*, *ibid.* **47**:95, 1927; *XLIV. The Role of the Thyroid and Parathyroid Glands in the Chemical Differentiation of Bone During Growth (Ash, Organic Matter and Water)*, *J. Biol. Chem.* **72**:505, 1927.

27. Kunde, M. M., and Williams, L.: *Studies on Experimental Cretinism: II. Nutritional Disturbances of Bones*, *Proc. Soc. Exper. & Med.* **23**:814, 1926.

28. Fahr, T.: *Endocrine System in Osteogenesis Imperfecta*, *Virchows Arch. f. path. Anat.* **261**:732, 1926 (*Child Devel. Abstr.*).

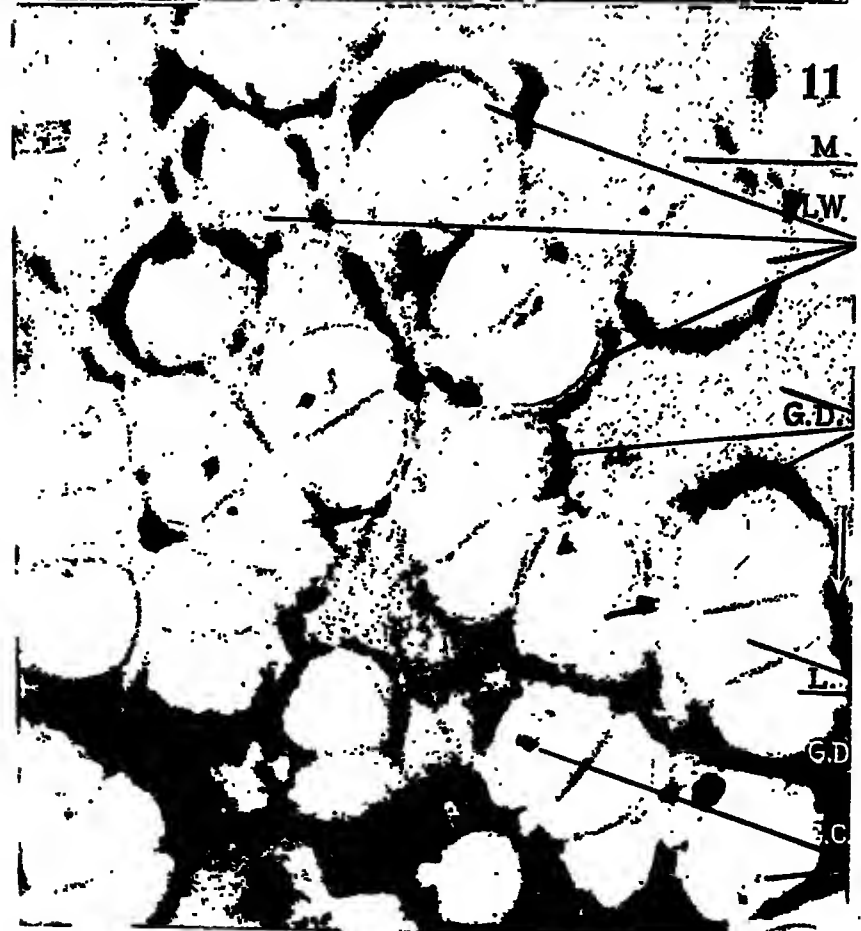


PLATE IV

changes are the fundamental factor causing dysfunction of the osteoblasts. By means of x-ray examinations on the living, Engelbach and McMahon<sup>29</sup> also showed marked changes in bone in various endocrine disorders. It is the general belief that hormones act on the cells of a tissue, which is much more probable, especially in the case of bone, than any hypothesis as to a chemical action on the matrix and its calcium content.

In a similar way vitamins are supposed to act on the cell, and McCarrison<sup>30</sup> showed marked changes in bone in cases of vitamin deficiency. In addition, Miles and Feng<sup>31</sup> studied many cases of osteomalacia in China and came to the conclusion that it is a deficiency disease due to lack of fat-soluble vitamins. They noted that there might be a calcium deficiency in the diet and in the blood at the same time, but this was not always so. Without a deficiency of calcium in the body, such a condition as osteomalacia can be conceived of only as a disease in which the bone cell is at fault. It was also noted that administration of cod liver oil caused bone growth for more than two months after the cessation of treatment.

The normal growth of bone and the deposition of a proper calcium content in its matrix is stimulated by sunlight and by ultraviolet light in cases of rickets. This surely must occur by action on the tissue cells of the bone. In a review of the causes of rickets, Tisdall<sup>32</sup> pointed out that a deficiency in the calcium content of the body is not sufficient in itself to cause this disease, whether the calcium is deficient either from diminished intake or from increased loss. A deficiency of vitamins alone or of phosphates alone will not produce rickets, but this deficiency leads only to osteoporosis by a failure to produce as large and heavy an amount of bone as necessary. Either a deficiency of calcium or a deficiency of phosphates combined with a deficiency in vitamins does, however, produce typical rickets. Robison and Soames<sup>33</sup> obtained similar results in experiments on rats. As every change in the various conditions already cited, except the deposition of the calcium in the bony matrix, is admittedly due to the activity of the bone cells, it seems reasonable to suppose that the deposition of calcium might also be ascribed to the cell's activities, as it occurs in such close correlation with

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29. Engelbach, William; and McMahon, A.: *Osseous Development in Endocrine Disorders*, *Endocrinology* 8:109 (Jan.) 1924.

30. McCarrison, R.: *Studies in Deficiency Disease*, London, Henry Frowde and Hodder and Stoughton, 1921.

31. Miles, L. M., and Feng, C.: *Calcium and Phosphorus Metabolism in Osteomalacia*, *J. Exper. Med.* 41:137, 1925.

32. Tisdall, F. F.: *The Etiology of Rickets*, *Canad. M. A. J.* 11:934 (Dec.) 1921.

33. Robison and Soames (footnote 15, fifth reference).

It may be presumed that all the cartilage cells can excrete soluble phosphates and carbonates, yet calcium deposits do not surround all cells, but only those of one definite, particular zone.

If the cartilage cell secretes the calcium into the matrix, how does it accomplish it? Granules of the salts are not visible in the cell or its lacuna or passing through the capsule. The lacunae in cartilage are closed spaces, not a series of intercommunicating passages or canals through the cartilage, so one cannot look on them as open pathways conducting calcium salts in solution which might diffuse into the matrix and precipitate.

There are no blood vessels or lymph channels leading to individual cell lacunae in cartilage, and the common idea is that cartilage cells obtain all needed nutrient by imbibition of dissolved substances which diffuse through the matrix.

If, therefore, the cell obtains a supply of calcium it does so in dissolved form by diffusion through the same matrix in which the deposition is later made in solid form. This disposes of any view that the salts are excreted in liquid form and then precipitated in the matrix by lowering of carbon dioxide content, for the same matrix would have to possess a constitution which would allow calcium to pass in solution into the cells but not out again without being precipitated; this appears absurd. That there is calcium in the cartilage cells has also been demonstrated by Rabl.<sup>2</sup>

In studying the precipitation of calcium phosphate and carbonate in colloids in vitro, I noted a significant fact. With similar concentrations of reagents, it was more difficult to produce precipitation of the calcium salts in aqueous extracts of cartilage than in any other medium employed. There was always a much smaller quantity of precipitate obtained in these cases. This forms a strong argument against the view that cartilage calcifies by a simple precipitation reaction. Bechhold<sup>3</sup> also noted that cartilage shows a selective adsorption of calcium.

From experiments on puppies, Jones<sup>4</sup> concluded that two factors influence calcification. The more important one is the metabolic state inherent in the animal, and the other is diet, which influences the metabolism of the cells. The balance of ions between the bone-forming cells and their surroundings determines the deposition of bone salts. Any agent changing the metabolism of the bone cells will alter this ionic balance and will influence the deposition or the absorption of bone.

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2. Rabl, R. H.: Ueber die Kalkablagerung bei der Knochenentwicklung, *Klin. Wchnschr.* 2:1644, 1923.

3. Bechhold, H.: *Colloids in Biology and Medicine*, translated by J. G. M. Bullowa, New York, D. Van Nostrand Co., 1919.

4. Jones, Martha R.: Studies on Inorganic Salt Metabolism: III. On Certain Factors Which Influence the Deposition and Resorption of Bone, *Am. J. Physiol.* 79:694, 1926-1927.



all the other activities. Medes<sup>34</sup> showed that the bones of rats on a diet poor in phosphorus exhibit rachitic changes, while diets low in calcium content lead only to osteoporosis.

It is to be particularly noted that cells having to do with the special use of calcium for structural purposes are not all of one kind. Three types of epithelium are found capable of secreting calcium to form solid structures: namely, the epithelium of the mantle of the clam, the epithelium of the shell gland of the bird, and that of the enamel organ of the tooth. Three types of connective tissue cells are similarly concerned: the cartilage cell, the osteoblasts and bone corpuscles and, finally, the odontoblasts of the teeth.

The view is readily accepted that the shell of the clam and the shell of the bird's egg are products of secretion, both the organic matrix and the calcium salts being present through the secretory function of the cells. It is generally admitted also that the organic matrix of bone and cartilage and of the enamel and dentine of the tooth are products of the cell. In the latter cases, why should not calcium also be present because of the secretory activity of the cells?

#### SUMMARY

*Development of Bone.*—1. Intramembranous bone develops by the simple calcification of a fibrous matrix, osteoblasts gradually walling themselves in with a finely granular deposit.

2. The formation of endochondral bone shows a progressive series of marked changes. The cells in the cartilage that are about to change enlarge, and the matrix increases in quantity and stains poorly. The cartilage cells then become segregated into groups between which lie the main, heavy trabeculae, and the matrix again stains deeply and calcifies by deposition of granules.

Blood vessels bearing osteoblasts now invade the calcified cartilage, eroding the narrower trabeculae and occupying the lacunae, from which the cartilage cells have disappeared. Osteoblasts deposit true bone on the remaining trabeculae; this first bone and the calcified trabeculae on which it lies are later reorganized, and an arrangement better suited to the structure as a whole is laid down.

A calcified cartilage skeleton, temporary in duration and replaced by bone, is an evolutionary phenomenon and repeats in the individual the history of the race.

Endochondral bones of different shapes and sizes show individual modifications in their process of development.

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34. Medes, G.: Rats on Diets High in Phosphorus and Low in Calcium, *Proc. Soc. Exper. Biol. & Med.* 23:679, 1926.

A definite proportion was shown by Wells<sup>5</sup> to exist between the amount of calcium carbonate and phosphate in bone and calcified cartilage. In normal persons, there are fifteen parts of calcium carbonate to eighty-five parts of calcium phosphate, or in the chemical proportions of one molecule of the carbonate to three of the phosphate.

The salts present in bone have been recently analyzed by Howland, Marriott and Kramer.<sup>6</sup> They concluded that calcium is present only in the form of neutral calcium carbonate and tricalcium phosphate. The ratio of phosphate to carbonate depends directly on the amount of phosphates in the blood serum and is therefore lower in rickets, in which the phosphorus content is markedly reduced, than it is in health. In artificial mediums the ratio of phosphate to carbonate in the precipitate is in direct proportion to the quantities dissolved in the mediums, and can be obtained in the same relative amounts as in bone. However, the authors stated that the latter fact must not be taken to indicate that calcification is a process of simple precipitation, as they have shown that other factors have to be taken into account.

Shipley, Kramer and Howland<sup>7</sup> took slices of cartilage from developing bones and immersed them in solutions containing calcium salts, where they were then incubated. Calcification of the cartilage occurred in nine hours with normal blood concentrations of calcium and phosphorus and at the normal hydrogen ion concentration of serum. This calcification was always in the matrix, never in the cells, and was not on the surface of a slice, but always in the depths of its thickness. Microscopic examination did not show any differences from the calcification of cartilage seen during normal development of bone.

Costochondral junctions in children dying of rickets did not calcify in rachitic serum, but the process did occur when they were immersed in normal serum.

Calcification did not occur after the cartilage was boiled or after the use of antiseptics or protoplasmic poisons. This clearly indicates the active part which the cell must play in the process.

With the addition of 1 per cent of egg albumin to the solutions, calcification did not occur in forty-eight hours, but if the slices of cartilage were washed at the end of twenty-eight hours and placed in fresh solutions without albumin calcification took place. This indicates that calcium when bound to a protein is not easily utilized by the cell,

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5. Wells, H. G.: *Pathological Calcification*, J. M. Research 9:491, 1906; *Calcification and Ossification*, Harvey Lectures, 1910-1911; *Calcification and Ossification*, Arch. Int. Med. 7:721 (June) 1911; *Chemical Pathology*, ed 3, Philadelphia, W. B. Saunders Company, 1918.

6. Howland, John W.; Marriott, McKim and Kramer, B.: *Studies Upon the Inorganic Composition of Bone*, J. Biol. Chem. 68:721, 1926.

7. Shipley, P. G.; Kramer, B., and Howland, J.: *Studies upon Calcification in Vitro*, Biochem. J. 20:379, 1926.

(a) Long bones are invaded at the center of the shaft by blood vessels which bud and grow rapidly and carry in osteoblasts with them. Calcified cartilage always lies just ahead of the vessels and is continually invaded and its line pushed back until the whole shaft is ossified. The calcified cartilage grows away from the entering vessels. Blood vessels are not present in the shaft before the process of ossification begins.

(b) Epiphyses and short irregular bones such as the carpals and tarsals contain blood vessels long before ossification begins. These vessels extend about half way to the center and then branch and anastomose. The central area bounded by them calcifies and is then invaded by budding vessels carrying in osteoblasts. The cartilage is eroded except for some larger trabeculae; the zone is ossified and then extends its boundaries until it reaches the periphery of the bone. In this case the calcified cartilage extends toward the entering blood vessels, not away from them as seen in the shafts of long bones.

(c) Endochondral bones of the skull may show enlargement of the cartilage cells and calcification of the matrix without the presence of any blood vessels until the moment when they are penetrated by budding vessels accompanied by osteoblasts.

*Form of Calcium Deposits.*—1. In Cartilage: The deposit is always in the form of distinct granules which accumulate in closely packed masses but do not fuse. The granules appear first in the matrix immediately around the cartilage cells, but there appears to be a thin envelop or capsule forming the actual wall of each lacuna which is free from granules. The granules appear first around those cells nearest to blood vessels.

2. In Bone: The deposit is always granular. The granules are minute, much smaller than those in cartilage, and they may fuse to form a homogeneous mass. The granules appear first in the matrix in immediate contact with the osteoblasts.

*Manner of Deposition of Calcium Salts.*—In normal calcification of cartilage and bone, the deposition of the calcium salts is presumed to be due to cellular activity, because the first evidence of deposition is always immediately about the cell and can occur only after definite changes in the cell and in the organic matrix formed by it (Watt). It has also been shown that precipitation of calcium salts is difficult in a cartilage extract (Watt<sup>18</sup>), and solutions of calcium phosphate in conditions similar to those in the tissues can exist for a long period without precipitating (Holt, LaMer and Chown<sup>19</sup>) and normal blood is 200 per cent saturated.

Slices of normal living cartilage will calcify rapidly when incubated in proper solutions, but will not do so if the cells are killed (Shipley, Kramer and Howland<sup>7</sup>). Cells forming the enamel and dentine of the

and that it is the ionized calcium in the blood serum which is readily available for calcification.

That part of the calcium in the blood serum is not ionized and is bound to some protein was demonstrated by Marrack and Thacker,<sup>8</sup> who also showed that a change of hydrogen ion concentration of from 7.4 to 7.8 reduces the calcium ion concentration 60 per cent. In regard to the latter point the work of Jones is significant, as she showed that destruction of bone in rickets is much greater as the alkalinity of the tissues is increased by appropriate diets and healing tends to occur with the administration of acids.

A nondiffusible, nonionizable portion of the calcium in the blood, bound to a protein component, was also shown by Updegraff, Greenberg and Clark,<sup>9</sup> and by Hastings, Murray and Sendroy.<sup>10</sup>

Freudenberg and György<sup>11</sup> expressed the belief that in some way calcium is bound to the protein constituent of the cartilaginous matrix and reacts with phosphates and carbonates to form the hard deposit evident in calcification. Products of tissue degeneration as well as urea and ammonium salts prevent calcification. The phosphate and carbonate formed may secondarily split off as inorganic salts from the protein and leave the latter free to repeat the process, thus increasing the calcification.

According to Bergeim, rachitic rats lose both calcium and phosphorus in the feces, while normal animals absorb these elements. Therefore, rickets is not only a pathologic condition of the bone but shows derangement of other parts of the body. Telfer<sup>12</sup> demonstrated similar conditions in human beings and showed that administration of cod liver oil caused great increase in absorption of both calcium and phosphorus.

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8. Marrack, J., and Thacker, G.: *The State of Calcium in Body Fluids*, *Biochem. J.* 20:580, 1926.

9. Updegraff, H.; Greenberg, D. M., and Clark, G. W.: *A Study of the Distribution of the Diffusible and Nondiffusible Calcium in the Blood Sera of Normal Animals*, *J. Biol. Chem.* 71:87, 1926.

10. Hastings, A. B.; Murray, C. D., and Sendroy, J., Jr.: *Studies of the Solubility of Calcium Salts: I. The Solubility of Calcium Carbonate in Salt Solutions and Biological Fluids*, *J. Biol. Chem.* 71:723, 1926. Sendroy, J., Jr., and Hastings, A. B.: *II. Solubility of Tertiary Calcium Phosphate in Salt Solutions and Biological Fluids. III. Solubility of Calcium Carbonate and Tertiary Calcium Phosphate Under Various Conditions*, *J. Biol. Chem.* 7:783, 1926.

11. Freudenberg, E., and György, P.: *Kalkbindung durch tierische Gewebe*, I to X *Biochem. Ztschr.* 110:299, 1920; 115:96, 1921; 118:50, 1921; 121:131, 1921; 121:142, 1921; 124:299, 1921; 129:134, 1922; 129:138, 1922; 142:407, 1923; 147:191, 1924.

12. Telfer, S. V.: *Studies in Calcium and Phosphorus Metabolism: IV. The Influence of Free Fatty Acids in the Intestine on the Absorption and Excretion of the Mineral Elements. V. Infantile Rickets. The Excretion and Absorption of the Mineral Elements and the Influence of Fat in the Diet on Mineral Metabolism*, *Quart. J. Med.* 20:1, 1926.

teeth show a definite storage and direction of transport of trypan blue and bone cells show similar activities (Blotevogel<sup>23</sup>).

Secretions of the ductless glands exert a marked influence on growth of bone, and cell tonics such as sunlight, ultraviolet light and vitamin also show marked effects. Bone and calcifying cartilage are shown to possess a ferment, esterase, which will convert organic phosphates into inorganic compounds (Kay and Robison<sup>16</sup>).

Collateral evidence of the power of cells to secrete calcium salts to form hard structures is shown by the epithelium of the mantle of the clam in producing the clam shell and the epithelium of the shell gland in producing the shell of the bird's egg.

Bones become rarefied when blood calcium is low, as in pregnancy and in increased loss from the body in certain fistulas. There seems to be a calcium balance between blood, bone cell and bone matrix something like the sugar balance in the liver.

All the foregoing points seem to point toward cellular activity in the calcification of bone and cartilage. Thus, six types of cells can secrete calcium to form hard structures: three epithelial cells—the ameloblast which builds enamel of the teeth, the epithelium of the mantle of the clam, and the epithelium of the bird's shell gland—and three types of connective tissue cell—the odontoblast which builds dentine in the teeth, the cartilage cell, and finally the osteoblast and bone corpuscle.

In the later stages it was found that the stump again assumed its normal color and had areas which showed crepitation, but the site that was exposed was found firmly adherent to the nearest portion of the wall of the chest. The strands of compression near the suture and also flattening of the bronchioles were seen microscopically. Some bronchioles lost their major characteristics and could be recognized only by the cartilage or the remnants of bronchial epithelium. In some areas an entire loss of alveolation was found, and the whole field contained dense fibrous tissue. In the crepitating areas, the characteristic alveolation but also a characteristic increase in the interstitial fibrous tissue



Fig. 3.—Section from the stump eighty-one days after lobectomy. The strand formation of the alveoli caused by the silk suture should be noted.

with proportional decrease in the size of the alveolar spaces have been found.

In the presence of infection, changes characteristic of pneumonia were noticed as well as areas in which there was a localized deposition of polymorphonuclears but no destruction of the center. In such cases, lobar pneumonia in the contiguous lobe and even on the opposite side was also noticed.

In all cases, a thickening of the pleura around the stump was found. This thickened pleura and the adhesions are the best allies in giving good results.

The contiguous lobe or the lung on the opposite side may show any of several changes. It may remain normal; it may show lobar pneumonia, edema, and, most frequently, an interstitial thickening.

Secondary operations on the same or opposite side have not been borne well by these dogs. It is possible that the anesthetic has something to do with it. Ether has been used throughout. One animal, which was thought to have recovered completely, was operated on 101 days after the first operation. This dog died on the table in the middle of the operation. It did not take the anesthetic well in spite of the satisfactory anesthesia and artificial respiration.

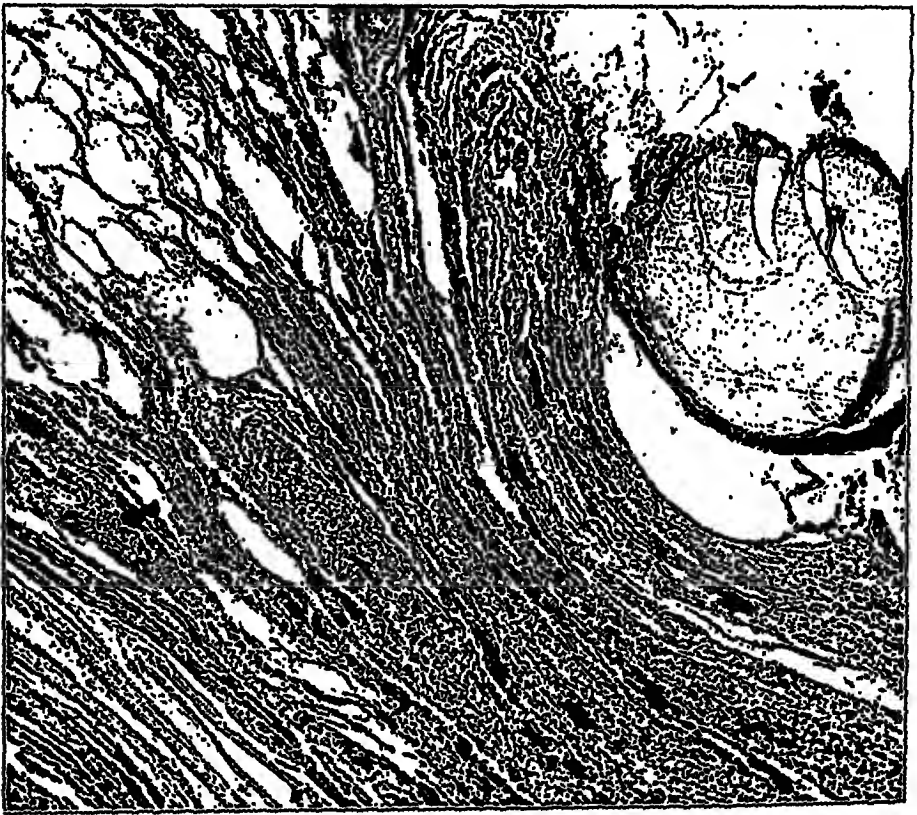


Fig. 4.—Section from the stump 101 days after lobectomy. The strand formation of the alveoli at the point of compression and the gradual return to normal alveolation beyond the catgut suture should be noted.

#### COMMENT

The results in these experiments were encouraging. In only one case were infection and leakage of air at the stump encountered. In all the others, the stump remained airtight and watertight. It was noticed that when the dogs were left alone after the operation they might live indefinitely, if they survived the first six days. It is possible that the removal of a lobe or the whole lung will cause a definite strain on the circulation, with a subsequent acute or subacute edema which eventually causes asphyxia in the dog. Moreover, if the wall of the chest is left

# OXYGEN IN THE TREATMENT OF POSTOPERATIVE BRONCHOPNEUMONIA \*

MELVIN W. BINGER, M.D.

Fellow in Medicine, The Mayo Foundation

E. STARR JUDD, M.D.

ALEXANDER B. MOORE, M.D.

AND

RUSSELL M. WILDER, M.D.

ROCHESTER, MINN.

In the symposium on treatment with oxygen in cases of pneumonia that was presented last year at the meeting of the Association of American Physicians, Binger,<sup>1</sup> Barach<sup>2</sup> and Boothby<sup>3</sup> suggested that the disrepute of such treatment could be accounted for by the ineffectiveness of former methods of administering the oxygen. They then described the newer apparatus, the oxygen chamber and the oxygen tent, by means of which it is possible to envelop the patient, or his head, in an atmosphere of any concentration of oxygen desired. They demonstrated that with atmospheres of about 50 per cent oxygen, anoxemia could usually be controlled, and the patient with pneumonia improved subjectively; the temperature and pulse often fell dramatically.

The present report is concerned chiefly with the treatment with oxygen in cases of postoperative pneumonia at The Mayo Clinic. Up to Jan. 1, 1927, oxygen had been used in only a few cases, but by this time a fleet of tents had been put into service, and approximately 50 per cent of the patients in whom pneumonia developed in 1927 were treated with oxygen. Therefore, if such a procedure has definite merit, it should be reflected in the mortality statistics of this year. The following data were noted:

In 1927, the pathologist named pneumonia as the cause of death in thirty-six of the postoperative cases which came to necropsy. During the preceding four years, there had been an average of forty-eight deaths, with a fluctuation, however, of from thirty-nine to fifty-six.

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\* Read before the Association of American Physicians, Washington, D. C., May 1, 1928.

\* From The Mayo Clinic, Rochester, Minn.

1. Binger, C. A. L.: General Considerations in Regard to Oxygen Therapy, Tr. A. Am. Phys. 42:301, 1927.

2. Barach, A. L.: Acute Disturbance of Lung Function in Pneumonia, Tr. A. Am. Phys. 42:303, 1927.

3. Boothby, W. M., and Haines, S. F.: Oxygen Therapy, Tr. A. Am. Phys. 42:287, 1927.



*Malacoplakia.*—Berg<sup>51</sup> reported a case of malacoplakia of the bladder which had been under treatment since 1907, at which time the patient had passed two stones 0.3 cm. in diameter. The diagnosis was made by cystoscopic examination. The patient returned eighteen years later with calculous pyonephrosis on the right side. Nephrectomy was followed by uneventful convalescence. Cystoscopy three months later revealed the same picture in the bladder as had been noted eighteen years previously, except that the areas were slightly smaller and better defined. Berg believed that the process resulted from irritation due to the stones. The plaques themselves did not cause symptoms.

[ED. NOTE.—Several reports on malacoplakia of the bladder have appeared recently. Certain writers have suggested that they are a precancerous condition, others that they cause many vague symptoms. This report of Berg is interesting in that it suggests that malacoplakia may be an entirely innocuous condition.]

Grieg<sup>52</sup> reported a case of a multipara, aged 30, with a suprapubic tumor which had grown large over a period of eight months. It was smooth, oval and painless, was not freely movable, and did not fluctuate. It lay between the umbilicus and symphysis. Pain in the loin, radiating to the thigh was present. With the assumption that a uterine or ovarian tumor was present, laparotomy was undertaken. The tumor was extra-peritoneal and easily isolated. There was no connection with the umbilicus, although there was a connection between its lower pole and the bladder. The patient was living and well seven years after removal of the tumor. Microscopically, the tumor was found to be a spindle cell sarcoma.

Twenty malignant tumors of the urachus were also noted; eight deaths followed surgical removal. Twelve of the twenty tumors were carcinomas and eight were sarcomas.

*Contracture of the Neck of the Bladder.*—Knorr<sup>53</sup> reported two cases of sclerosis and four of contracture of the neck of the bladder in women. The former ran a chronic course, resulting finally in repeated attacks of urinary retention. In both of these cases there had been a previous inflammatory condition of the neck and the trigone of the bladder, in one case due to staphylococcus and in the other to the colon bacillus. In the cases of contracture, which is a condition of muscular cramp, cystitis of the neck and trigone was also an etiologic factor.

51. Berg, G.: Zur Malakoplakia vesicae, Verhandl. d. deutsch. gesellsch. f. urol., 1927, p. 306.

52. Grieg, D. M.: Report of a Case of Sarcoma of the Urachus, Edinburgh Med. J. 34:425, 1927.

53. Knorr, R.: Ueber Kontraktur und Sklerose des Blasenhalsses beim Weibe, Zentralbl. f. Gynäk. 51:1154, 1927.

In 1927, sixteen deaths were attributed to pneumonia in cases in which operation had been performed on the stomach or duodenum. Usually the diagnosis was made at necropsy by the pathologist; sometimes it was made by the surgeon. In the preceding year (1926), when little oxygen was used, the number of deaths from pneumonia in the corresponding group of cases was twenty-two. The deaths from all causes following operation on the stomach and duodenum fell from sixty-two in 1926, to fifty-three in 1927, a reduction of the mortality rate of 20 per cent, chiefly attributable to fewer deaths from pneumonia (table 1).

In the hospital in which most operations of the upper part of the abdomen were performed, the deaths from pneumonia diagnosed at necropsy in 1927 were twelve (in 8,124 operations) as opposed to

TABLE 1.—*Operations on the Stomach and Duodenum*

Year	Operations (Cases)	Deaths, All Causes		Deaths from Pneumonia	
		Cases	Per Cent	Cases	Per Cent of All Deaths
1926.....	1,393	62	4.45	22	36
1927.....	1,482	53	3.57	16	30

TABLE 2.—*Comparative Mortality in Two Hundred and Five Cases*

Treatment Started, Days After Operation	Cases	Deaths, All Causes		Deaths, Pneumonia Cases
		Cases	Per Cent	
1 to 4.....	159	10	12	4
5 or more.....	47	35	74	18

twenty-two (in 7,866 operations) in 1926. Oxygen had not been used in three of the twelve cases in 1927, and it had been resorted to tardily in six cases. Only three of these deaths can be attributed to failure of treatment with oxygen.

We observed 205 cases of postoperative pneumonia in which the patients were treated with oxygen. The diagnosis was confirmed in most instances by roentgenograms. If this series of cases is divided arbitrarily into those in which treatment with oxygen was started before the fifth day after operation, and those in which it was started after the fourth day, it is shown that the mortality in the latter group is six times as high as that in the former group: 74 per cent as opposed to 12 per cent (table 2). The fourth day after operation is late in many cases, since evidence of the onset of pulmonary complications can usually be detected within the first twenty-four hours after operation and the condition of the patients may be serious much earlier than the fourth day.

Slow and cautious dilatation of the sphincter is the suitable treatment in most cases.

Frühwald<sup>54</sup> found in a series of 1,300 endoscopies 372 cases of lesions at the neck of the bladder due to infection. Most of the patients were women. Specific urethritis was present in 42 per cent of the cases. The type of changes are: (1) in from four to six weeks following infection small nodules with circumscribed edema can be seen; these may disappear spontaneously; (2) in three months small filiform and transparent efflorescences appear, and (3) in four months polyps of various sizes, shape and form (finger-like, club-like, cock's comb-like, forked, and cauliflower-like) appear. These polyps are occasionally the underlying cause of resistant gonorrhea; they are found even though the gonococcus is not present, and they may be the cause of persistent infection after apparent cure. These changes could only be found in 4 of 171 control cases in which there had never been any sign of gonorrheal infection. Etiologically, gonorrhea plays the chief, but not the only part. Histologic examination shows that possibly these polyps are developed from preformed epithelial nests which multiply by irritation, usually the result of gonorrhea.

*Lesions of the Nerves.*—McCrea<sup>55</sup> concluded that the vesical symptoms of tabes are of two chief clinical types: the incontinent, in which there is a definite cutting off of sensation from the higher centers, and the parietic, in which the sensory loss, although present, is not so apparent, being concealed by the interference with reflex function of the viscus. A third type exists in which the symptoms are mixed, but this type is rare. In the parietic bladder, the more prominent symptoms are due to interference with the reflex function of the organ, and are largely the result of lesions of the afferent fibers running in the autonomic pelvic nerves. In the incontinent bladder, the most obvious symptoms are similar to those of a lesion of the sensory pathway in the cord, and this sensory loss is significant in the production of muscle senses which are transmitted by the pudic nerves.

McCrea suggested that tabes may rarely affect the autonomic or visceral nerves and the somatic sensory nerves simultaneously, and if it does, never to the same degree. This explains the difference between the pelvis and pudic nerves. The most obvious cases of tabes are those presenting destruction of somatic sensory fibers, but not visceral crises.

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54. Frühwald: Veränderungen am Orificium internum urethrae bei Gonorrhoe der Frau, *Dermat. Wchnschr.* 84:376, 1927.

55. McCrea, E. D.: Bladder in Tabes, *Irish J. M. Sc.*, 1927, p. 658.

It is recognized that these data do not constitute biometric proof of the efficiency of treatment with oxygen. Nevertheless, in view of the fact that the treatment was given in not more than 50 per cent of all cases of postoperative pulmonary complications, that in many of these the oxygen was administered late, and that there were no other significant innovations in the treatment of patients before or after operation in 1927, we feel justified in concluding that lives have been saved.

In an endeavor to obtain other evidence of the value of the procedure, we resorted to experiments on animals. Smith<sup>4</sup> recently reported that he had caused aspiration pneumonia in guinea-pigs and rabbits by the intratracheal injection of infected material. Dogs are resistant to such procedures, as Cutler and Schlueter<sup>5</sup> have noted, but the guinea-pig proves to be surprisingly sensitive. By anesthetization with ether, exposure of the trachea by operation and intratracheal injections, we produced pneumonia almost constantly with streptococci freshly cultured from healthy throats. Furthermore, the pneumonia almost always proved fatal, most of the animals dying from extensive bronchopneumonia within two weeks. A series of such experiments was conducted. In each experiment, ten or twelve guinea-pigs were anesthetized and inoculated in an identical manner, and then half of them were subjected immediately after the operation to an atmosphere of 50 per cent oxygen and left in this atmosphere for twenty-four or forty-eight hours. The results encourage us to believe that oxygen properly administered is a life-saving measure. Sixty-six of seventy untreated guinea-pigs died within two weeks. Six of fifty-one treated guinea-pigs were killed from the second to the sixth day for examination of the lungs; twenty-two guinea-pigs died and twenty-three survived. The mortality of the treated guinea-pigs is, thus, at least 50 per cent less than that of the untreated guinea-pigs.

During the last four months, in selected cases on one of the surgical services, treatment with oxygen has been started immediately after operation and continued for from twenty-four to forty-eight hours. The patients chosen were those who had had recent colds, who were elderly or feeble, or who had been operated on in the upper part of the abdomen; in other words, they were patients concerning whom there was reason for apprehension in a consideration of postoperative pulmonary complications. Although this group was small, it is encouraging that pulmonary infection did not develop in a single instance.

4. Smith, D. T.: *Experimental Aspiratory Abscess*, Arch. Surg. 14:231 (Jan.) 1927.

5. Cutler, E. C., and Schlueter, S. A.: *The Experimental Production of Abscess of the Lung*, Ann. Surg. 84:256, 1926.

**Fistula.**—Roeder<sup>56</sup> pointed out that the interference with the blood supply of the lower part of the ureter and bladder following total hysterectomy, as a cause of postoperative ureteral and vesical fistula, deserves more consideration than it has received in the past.

The blood supply of the inner portion of the anterior vaginal wall and the apposed bladder comes from branches which originate from the inferior vesical and uterine arteries. The uterine arteries send branches to surround the vault of the vagina, the anterior branches uniting to form a single vessel which runs forward in the median line of the anterior vaginal wall. This is the *arteria azygos vaginae*. Large fistulas may result from blocking of these vessels in the performance of total hysterectomy.

In two patients treated by Roeder, so much bladder tissue was destroyed that it would have been impossible to approximate the edges even after extensive dissection. Roeder, therefore, made an incision in the vaginal walls through their entire thickness, starting 2.5 cm. or more from the fistula. Thick flaps were turned back to afford an ample supply of blood. These flaps of vaginal wall were dissected up to within 0.8 cm. of the margin of the fistula. The flaps were then united by several layers of chromic catgut sutures, the first suture being pulled through the wound of a previously performed suprapubic cystostomy and kept under slight tension to assist in coaptation of the vaginal flaps. The bladder was left open for drainage and a self-retaining catheter placed in the urethra. In the area remaining after the vaginal flaps had been turned into the bladder, a drainage tube was placed and brought to the surface paravaginally. This was done to prevent possible leakage of urine through the vagina and the reestablishment of the fistula.

The postoperative care involved irrigation of the urethral catheter twice daily; the irrigation was allowed to come through the suprapubic tube or wound. The drain inserted paravaginally was left in for about ten days. Results from the operation were satisfactory in both of Roeder's cases, although one of the patients died twelve days afterward from chronic nephritis and hepatitis. Necropsy showed that the bladder was firmly united at the site of repair.

Young<sup>57</sup> stated that the vaginal approach in operating on vesico-vaginal fistulas is not always satisfactory. He reported the case of a woman, aged 31, whose bladder was accidentally opened during the removal of a hydatid mole. Eleven operations over a period of three

56. Roeder, C. A.: A Technique for the Repair of Large Vesicovaginal Fistulae, *Surg. Gynec. Obst.* 45:102, 1927.

57. Young, H. H.: Repair of Vesicovaginal Fistula: Presentation of New Instrument, *Surg. Gynec. Obst.* 45:226, 1927.

## COMMENT

There is reason to believe that treatment with oxygen has resulted in the actual saving of life. The good results have occurred chiefly in the group of cases in which treatment was instituted reasonably early. Administration of oxygen immediately after operation and before the development of pulmonary lesion promises to be an effective method for preventing the occurrence of serious pulmonary complications.

years had been undertaken elsewhere in an attempt to close the fistula, but in each instance the wound had broken down and the fistula persisted. The patient's health was good and renal impairment was not demonstrable.

On examination, the uterus appeared to be normal. Slightly to the right of the median line on the anterior wall of the vagina was an area of induration with a slight depression in the center. On cystoscopy, about 20 cc. of clear urine was evacuated. The capacity of the bladder on forced distention was about 300 cc. The trigone was much distorted. Running forward and outward from the right side of the trigone was a peculiar band of tissue which was entirely separated from the wall of the bladder, except at its upper and lower ends; this bridge was entirely covered with mucous membrane. Beneath the band was the opening of the vesicovaginal fistula. The fistula could be seen from either the inner or the outer side of the bridge which spanned its orifice. The ureteral orifices could not be made out, but it was believed that the right orifice was near the fistula, and it did not seem wise to close the fistula by the vaginal route.

Suprapubic operation was carried out; the bladder was opened extraperitoneally in the median line and the orifice of the small vesicovaginal fistula was disclosed. The muscular bridge was excised. A small hook was made on the end of a large safety-pin. This was pushed through the fistula and then drawn outward. One side of the fistulous tract was impaled on the pin and drawn upward. The fistulous tract was then completely excised by a circular incision under vision. The large opening between the bladder and vagina was closed by means of purse string sutures placed through the bladder. The first layer was through the submucosa of the vagina and did not penetrate through the mucosa. This suture was of heavy chromic catgut and was tied through the bladder, thus securing complete closure of the vaginal opening. The next suture was of plain catgut treated with mercurochrome-220 soluble and approximated the musculature of the bladder; this left an irregular defect in the mucosa which was closed in a linear direction by means of a through-and-through plain catgut suture tied intraventrically. The insertion of these sutures, it is to be emphasized, was facilitated by the introduction of the index finger in the vagina to elevate the site of the fistula. The bladder was closed around a large Pezzer catheter.

During the earlier days of convalescence, the patient lay on the abdomen, face downward, as suggested by Chute. Young considered this an important detail. On the tenth day she was allowed to lie on her back, but the suprapubic catheter was kept in place for three

# A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

E. STARR JUDD, M.D.

ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.

ROANOKE, VA.

GORDON S. FOULDS, M.D.

TORONTO

JEAN VERBRUGGE, M.D.

ANTWERP, BELGIUM

AND

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

*(Concluded from page 898)*

## BLADDER

*Tumors.*—Beer,<sup>43</sup> at the Third Congress of the Society of International Urologists, stated that the employment of high frequency currents through the cystoscope has given excellent results in the treatment of tumors of the bladder. There are known differences in the action of the unipolar and bipolar current. The unipolar is more explosive and of a higher tension and requires greater amperage. The action of the bipolar current is more useful in producing extensive coagulation of the pedicle of a tumor. When the bladder is open, the papilloma may be held up with a clamp and the bipolar current allowed to penetrate through the tumor, which produces coagulation that extends through the pedicle in the adjacent wall of the bladder.

Beer has had excellent results in the endoscopic treatment of vesical tumors in 158 cases. In about 20 per cent of the cases, there were recurrences. Recurrences in the same site are usually due to insufficient destruction.

In the operative treatment of tumors of the bladder, Beer stated that it is necessary to prevent implantations of tumors. He suggested bringing the bladder outside the peritoneal cavity for a good exposure. The bladder should be opened with a radio knife and the various tumors coagulated and removed. Results with this treatment were satisfactory in thirty-three cases; 85 per cent of the patients were apparently cured. He has employed radium emanation planted through the cystoscope in sixteen cases with successful results in 50 per cent. The poorest results were obtained in cases of inoperable carcinoma situated in the

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43. Beer, M. E.: *Traitement des tumeurs de la vessie, par les agents physiques*, J. d'uroi. 24:327, 1927.



weeks. Complete recovery with healing of the fistula and good function of the bladder resulted.

Young described several instruments for thus impaling the fistulous tract and elevating it under the operator's view so that it may be carefully dissected out. A thin tractor with two spreading blades, similar to Young's prostatectomy tractor, but with delicate nonfenestrated blades, is suggested as a suitable instrument.

[ED. NOTE.—Vesicovaginal fistula is usually attacked from below through the vagina, possibly because of the success which first attended the operation of Sims. It is interesting to note that both Roeder and Young have recently reported operations by the transvesical route. Certainly the expedient appears favorable to those who have failed with this stubbornly recurrent condition. The surgical principles of removing the mucous membrane in such a way as to prevent its regrowth between the vagina and bladder is well established. Eversion of the mucosa of the vagina into the vagina away from the bladder and invasion of the mucosa of the bladder into the bladder away from the vagina in the process of closing the defect have been emphasized in contemporary literature. The transvesical approach, together with dependent drainage of the bladder during convalescence, seems theoretically to be satisfactory. The experience of Roeder and Young seems to show that their methods are practical.

*Tuberculosis.*—Ormond reported a case of severe tuberculosis of the bladder which failed to improve following right nephrectomy. The remaining kidney was almost totally without function. Inguinal ureterostomy relieved the patient greatly, and function in the remaining kidney was partially restored. Treatment consisted of local, general and medication for local effect. Numerous drugs have been recommended to be taken by mouth, such as methylene-blue, guaiacol in 5 mm. capsules, belladonna, hyoscyamus and oil of sandalwood. Heliotherapy, the use of tuberculin, general nutritional methods and drugs administered hypodermically are also recommended. Local treatment has varied greatly. Because irrigations are painful, instillations have been advocated. The following drugs have been used: mercuric chloride 1:5,000 to 1:1,000; iodoform in liquid petrolatum; 5 per cent guaiacol with iodoform in petrolatum; gomenol, from 10 to 20 per cent in oil; from 0.5 to 1 per cent picric acid; 5 per cent phenol; 1 per cent mercurochrome; 5 per cent silver nitrate; methylene-blue; iodine vapor and sterile air. Excision or fulguration of the ulcer is sometimes advised.

Four types of distressing intractable cases are cited in which further radical treatment is necessary: (1) bilateral renal tuberculosis;

region of the sphincter. In seventeen cases of carcinoma, deep roentgen-ray treatment was employed without any real cures. In certain cases, symptoms were ameliorated.

Löffler <sup>44</sup> reported twenty-two cases of resection of the bladder performed at the Krankenhaus in Vienna. Twenty of the operations were performed for carcinoma; one was performed for sarcomatous carcinoma, and one for ulcer. Most of the resections were carried out through a longitudinal suprapubic cystotomy opening under lumbar anesthesia produced with 5 per cent. tropacocaine. Ureters were reimplanted in cases of ureteral involvement. The immediate mortality was 27.3 per cent, and the late mortality 14.3 per cent.

Joseph <sup>45</sup> stated that the intravesical treatment of malignant vesical tumors is only an emergency measure which has been frequently employed because surgical measures have been so hopeless. The so-called resection of tumors of the bladder, that is, removing part of the wall of the bladder, has in general given poor results. From a great number of cases in the literature, it has been noted that there were recurrences following operation in from 80 to 90 per cent. In many cases, the patient's life is probably shortened by resection and made worse by tenesmus, fistula formation and more rapid growth and spread of the tumor. The only exceptions are the cases in which the tumors are in the dome of the bladder, the upper aspect of the anterior wall or the upper part of the posterior aspect. Tumors in these situations are technically easier to resect. If, however, as is often the case, the tumor lies in the floor of the bladder, in the neck, or between the ureteral orifices, satisfactory resections are not technically possible. Destruction and total extirpation of the bladder cannot be considered for such cases; the patient with a small tumor will refuse this treatment for a continuance of the small amount of suffering, while the patient who has a large growth, even though consenting to the operation, has only a small chance of recovery.

The resection of a tumor of the bladder is nevertheless considered because of the occasional cure in the dome of the bladder. This is an incomplete attempt at cure and is comparable to a supravaginal amputation of the uterus in carcinoma of the body of the uterus or the enucleation of carcinoma of the breast without amputation or resection of lymphatics. Consequently, Joseph employs intravesical treatment of malignant tumors. This manner of treating vesical tumors has given,

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44. Löffler, L.: Unsere Fälle von Blasenresektion, *Verhandl. d. deutsche gesellsch. f. urol.*, 1927, p. 361.

45. Joseph, E.: Die intravesicale Behandlung börsartiger Blasengeschwülste, *Verhandl. d. deutsche gesellsch. f. urol.*, 1927, pp. 323 and 364.

(2) tuberculosis of the remaining kidney, the other kidney having been removed for tuberculosis; (3) failure of the bladder to clear up following nephrectomy even though the remaining kidney is healthy, with the ureteral orifice becoming strictured and hydronephrosis resulting, and (4) advanced genital tuberculosis in the male. For treatment, the following methods have been brought forth: (1) complete excision of the bladder with implantation of the ureter into the intestine; (2) simple implantation of the ureter into the intestine; (3) implantation of the ureter to the skin of the groin, iliac or inguinal ureterostomy; (4) nephrostomy; (5) lumbar ureterostomy; (6) suprapubic cystotomy; (7) vaginal cystostomy, and (8) denervation of the bladder.]

Ormond<sup>58</sup> expressed the opinion that inguinal ureterostomy is the method of choice in most cases. It is easily performed, is short, relatively free from danger and the resulting fistula can be cared for satisfactorily.

*Syphilis.*—Gautier<sup>59</sup> reported a case of syphilis of the bladder. Several days after an injection of bismuth, frequency of urination and dysuria developed. On examination, a mass was felt above the prostate; this was situated in the median line and gave the same sensation as a vesical tumor. Cystoscopic examination revealed a large mass in the fundus of the bladder; its apex was an ulcerated crater. All signs and symptoms disappeared after extensive antisyphilitic treatment.

Gautier expressed the belief that the few preliminary injections of bismuth caused congestion of the bladder and attracted attention to that organ. He stated that cystoscopic examination should be performed in syphilitic patients who complain of any symptoms referred to the bladder.

*Paralysis.*—According to Boyd,<sup>60</sup> the dangers which come from overdistention of the bladder and their accompanying genito-urinary infections can be overcome in cases of acute paralysis of the bladder by suprapubic drainage. He stated that the objections to this procedure worth mentioning are few and that it has many advantages. The abdominal distention which so often exists and the lowered resistance of the tissues, due to paralysis of the abdominal wall, make certain precautions at operation necessary.

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58. Ormond, J. K.: Diversion of the Urine in Intractable and Incurable Vesical Tuberculosis, *J. Urol.* 19:109, 1928.

59. Gautier, M.: Gomme syphilitique de la vessie, *Presse méd.* 2:55, 1928.

60. Boyd, M. L.: Suprapubic Cystotomy in Bladder Paralysis, *J. Urol.* 18: 413, 1927.

he believes, satisfactory results. Aseptic tumors with only a few symptoms are excluded. Two methods are considered: thermocoagulation and chemicocoagulation. Joseph uses a combination of both. He covers the bleeding tumors with concentrated trichloroacetic acid (chemico-coagulation), using a ureteral catheter through the cystoscope. This treatment is comparable to treatment of inoperable carcinomas of the uterus with zinc chloride. A large part of the tumor sloughs off with this treatment, the tumor becomes smaller and then becomes covered with normal mucous membrane; bleeding and oozing are practically checked. At the next treatment, the necrotic material due to the former treatment has sloughed off and trichloroacetic acid is used again. In order to make this treatment more efficient, the thermocoagulation is followed by another treatment of trichloroacetic acid, which gives the acid an opportunity to penetrate into the tumor.

It is understood that cure cannot be obtained from the chemico-coagulation or from the thermocoagulation and chemicocoagulation. Joseph has, however, achieved long enduring results in some cases, noting that many patients have good health and ability to work even with an inoperable tumor. He has not observed benefit from radium or deep roentgen-ray therapy and stated that in the United States the urologists are getting away from radiotherapy.

Privess<sup>46</sup> stated that adenomas of the bladder are not common. He reported a case in which the patient came for treatment because of hemorrhoids, but gave a history of urethral stricture, vesical distress and urinary retention. Urethral dilatation and cystoscopy revealed smooth vesical calculi and a tumor, 2.5 cm. in diameter, covered with normal mucous membrane near the neck of the bladder. Cystotomy was performed with the removal of fifty stones and extirpation of the tumor. Histologically, the tumor was similar to prostatic tissue and it was thought to be of prostatic origin. Adenomas of the bladder are benign, and become serious only by causing retention or hemorrhage. The stones were probably formed because of the obstruction to urination.

Gagucan<sup>47</sup> divided tumors of the bladder into four groups: (1) true papilloma, (2) papilloma with malignant degeneration, (3) carcinoma and (4) massive carcinoma.

The treatment by deep roentgen ray, while not always producing cure, sometimes causes amelioration of symptoms and regression of the size of the tumor. The combined results of radium and roentgen ray

46. Privess, M.: Ueber gutartige Geschwülste der Harnblase: Ein Fall von Cystoadenoma papillare, *Trudy klinik voronežskaro universiteta*, 2:125, 1927.

47. Gagucan, M.: Des tumeurs vésicales, *J. d'uro.* 24:469, 1927.

**Foreign Bodies.**—Wolff<sup>61</sup> reported two cases of foreign bodies in the bladder; in a young girl, a hairpin was found, and in a middle-aged man a piece of chewing tobacco.

The diagnosis of foreign bodies can usually be made from the history. The symptoms are usually those of cystitis. Cystoscopically, besides foreign body, the mucous membrane of the bladder is diffusely red and the blood vessels are infected.

Treatment may be either conservative or radical, depending on the circumstances.

#### PROSTATE

**Hypertrophy.**—Hunt<sup>62</sup> stated that the combined efforts of surgeon and clinician are more essential in the treatment of diseases of the prostate than of most other diseases. Serious organic disturbances are sometimes associated with prostatic obstruction, and, although the obstruction may be the first consideration, the coincident organic disease must also be considered in the care of the patient.

One of the most important coincidental conditions met is cardiovascular disease. Willius reviewed the records in 705 cases of enlarged prostate and noted cardiovascular disease in 42 per cent. Arteriosclerotic disease occurred most frequently (43 per cent). Arteriosclerosis associated with hypertension occurred in 36 per cent. In 8 per cent of the cases, angina pectoris was present. The incidence of cardiovascular disease is higher with prostatic obstruction than with many other diseases during the same decades, suggesting that coexisting cardiovascular disease is aggravated by persistent urinary retention.

The frequency of this association emphasizes the necessity for careful examination of the heart in all prostatic cases. Electrocardiographic studies are indispensable. Prostatectomy should not be performed in the presence of malignant hypertension, except under unusual circumstances. Most such patients live less than two years, and only 10 per cent live five years.

Renal complications must also be dealt with in the treatment of prostatic obstruction. The most common complications are insufficiency and infection; the latter is unquestionably a contributing factor in the production of the former. With drainage of the bladder and adequate treatment, the infection usually subsides. It often reappears after prostatectomy, especially when the preoperative treatment has been inadequate or too brief, and it may be the cause of death.

61. Wolff, E. P.: Zur Kasuistik der Blasenfremdkörper, *Ztschr. f. urol. Chir.* 23:428, 1927.

62. Hunt, V. C.: Reduction of Mortality Rate in Benign Prostatic Hypertrophy, *J. Iowa State Med. Soc.* 18:86, 1928.

are much more satisfactory. The best results have been observed in the treatment of papillomatous tumors. Gagucau believes that surgical treatment still gives the best chance for cure, especially in cases of malignant tumor. Combination of surgical treatment with cautery and radium increases considerably the chances of success in the treatment of infiltrated carcinoma of the bladder.

Cassuto<sup>48</sup> reported a case of pyonephrosis resulting from obstruction to the lower part of the ureter. The patient had had urethritis for two years and occasional attacks of hematuria and pyuria. Cystoscopic examination revealed a papilloma about 3 cm. in diameter on the edge of the right ureteral orifice and closing it almost entirely. The tumor was destroyed by fulguration. One month afterward, the symptoms still continued. A right pyelogram revealed extensive pyonephrosis; drainage was instituted.

Herman<sup>49</sup> reported a case of neoplasm of the trigone of the bladder. The patient, a man, aged 70, gave a long history of urinary disturbance, including dysuria, difficulty and a small stream. Hematuria had been present for six months. The results of the general examination were negative. Rectal examination did not reveal enlargement of the prostate. It was impossible to pass a cystoscope because of an intravesical mass. A water-dilating cysto-urethroscope revealed a normal urethra and vesical neck, and a mass in the trigone, which was lobulated and sessile.

At operation, a lobulated tumor was found occupying practically the whole trigone, with its major portion beneath the trigone. The overlying thin mucosa was incised in the long axis and was found to be friable in the region of the anterior declivity of the tumor. Immediately beneath the mucosal covering, a multilobular, well encapsulated, yellowish-white mass was exposed. This consisted of a number of individual lobules loosely bound together but well encapsulated as a whole. The gross appearance of the tumor was characteristic in miniature of hypertrophic prostatic tissue. The mass was about 3.75 cm. in the anteroposterior diameter, and 2.5 cm. slightly below the level of the trigone in its greatest width from side to side. Approximately 1.75 cm. of the mass projected above the trigone; the remaining 2 cm. was buried within and below the trigonal musculature. The main portion of the mass, comprising about two thirds of the growth, was deeply placed and well encapsulated so that it could be shelled out with surprising ease. There was considerable bleeding from the right anterior

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48. Cassuto, A.: *Uro-pyonephrose due à un papillome implanté sur le méat urétéral*, *Lyon. chir.* 24:253, 1927.

49. Herman, Leon: *Neoplasm of the Trigone Vesicae: a Probable Instance of Hypertrophic Changes in Aberrant Prostatic Tissue*, *J. Urol.* 19:291, 1928.

Experience has shown that the patient with prostatic obstruction is, as a rule, a poor subject for immediate operation. In 1925, 1,783 cases were reviewed in which suprapubic prostatectomy was performed at The Mayo Clinic between Jan. 1, 1913, and Jan. 1, 1925, with an average mortality of 5.5 per cent. The deaths occurring after prostatectomy were studied to determine the relationship between preoperative preparation and the mortality rate. It was shown that when patients, apparently in good general health and showing few, if any signs of renal injury were operated on immediately without preparation, there was a mortality rate nearly as great as in the group of patients in poor general health with marked renal insufficiency and infection, operated on only after adequate preparation. It has been three years since preoperative treatment has been instituted in all cases previous to prostatectomy at The Mayo Clinic. Before that time 37 per cent of patients, because of apparently good health and what appeared to be adequate cardiovascular renal reserve, were considered good subjects for the one-stage operation without any preliminary treatment. However, 44 per cent of the deaths after prostatectomy occurred in this group, and the mortality rate was 6.6 per cent. During the same period, 437 patients (24.6 per cent), considered the poorest subjects for operation, were treated by preliminary cystostomy and were adequately prepared before prostatectomy; the mortality rate in this group was 7.5 per cent. The remaining 38 per cent of patients, those with moderately impaired cardiovascular renal reserve, were treated by the installation of a permanent indwelling catheter until they were believed to be ready for operation. The one-stage suprapubic operation was used, and the mortality rate was 3.3 per cent.

The mortality rate is markedly influenced by the amount of preliminary treatment. During a period of one year in which preoperative treatment for a minimum of ten days was adopted in all cases, the following data were obtained: In 225 cases, there were 6 (2.3 per cent) deaths. A one-stage operation was performed in 188 cases with 4 deaths, a mortality rate of 2.1 per cent, as against a two-stage operation in 67 cases with death in 2, a mortality rate of 2.9 per cent.

Hunt stated that prostatectomy should never be performed without a period of preliminary treatment. In the majority of cases, satisfactory drainage can be obtained by a permanent indwelling urethral catheter. Vesical lesions, such as stones, diverticula and malignant tumors, associated with reduction of cardiovascular renal reserve, requiring a long period of preparation, still require cystostomy. Usually about 75 per cent of patients may be prepared by drainage through the urethral catheter.

Ether as a general anesthetic presents the greatest hazards in cases of prostatic obstruction, not in the administration, because it has a

segment of the bed of the tumor. This was controlled by packing and sutures, the latter being so placed that the interureteric bar was drawn forward to the trigonal mucosa. As the latter was necrotic and the underlying muscles atrophic, it was with some difficulty that the sutures were made to hold. The bed, on exploration bimanually, was found to be extensive, situated well above the prostate gland and sphincteric area, and to extend backward to the rectal wall, separated from the latter only by the capsule of the tumor.

The bladder was closed with drainage. Convalescence was uneventful for thirty-one days; the wound had closed with reestablishment of normal voiding. After the patient had been up for a week, he suddenly became stuporous and died in uremic coma within a period of twelve hours. The pathologic report on the tissue removed was "benign hypertrophy of the prostate gland."

There would not seem to be any question of the identity of the tumor, although certain vesical tumors classified as adenomas resemble in minute structure benign prostatic hypertrophy. The neoplasm apparently originated within or beneath the trigonal structures, and in its fully developed state was situated above the prostate gland, and at a considerable distance from the internal sphincter muscle. The normally situated prostate gland was not enlarged, and the position of the tumor and of the cavity from whence it came justified the conclusion that the tumor and the prostate gland were entirely unrelated anatomically. The question seemed to resolve itself into a differentiation of tumor originating from glandular tissue other than that comprising the prostate gland, of accessory glands in the region of the vesical outlet, and of benign hypertrophic changes in aberrant prostatic tissue.

Comparison with the growth and development of tumors known to have originated in the trigonal mucosal glands justified the conclusion that this tumor did not originate in these structures, but, in all probability, in structures beneath or within the trigonal musculature. The probabilities are that the tumor presented hypertrophic changes in aberrant prostatic tubules.

Deming<sup>50</sup> noted in the literature the reports of nine cases of primary carcinoma developing in diverticula of the bladder and reported one case of his own.

The age incidence in carcinoma and diverticula was between 57 and 70 years, most of the patients being close to the age of 62. All patients were men. All but one of the diverticula were infected. The diverticula were single; five were on the left side near the left ureteral orifice,

50. Deming, C. L.: Primary Carcinoma of Diverticulum of the Bladder, *J. Urol.* 18:73, 1927.



wider margin of safety than have other general anesthetics, but in the subsequent renal depression and acute pulmonary complications. Patients at the age when prostatectomy is usually performed are susceptible to the inhalation type of pneumonia and to bronchial troubles. Gas anesthetic, when skillfully administered, is usually satisfactory. Regional anesthesia minimizes the postoperative renal depression and pulmonary complications.

The successful management of prostatic obstruction necessitates regarding it from a general medical point of view as a systemic disease, not only by the urologist and the surgeon, but by the internist. The surgical principles involved in prostatectomy are significant, but so far as mortality is concerned Hunt believed that a poor operation after thorough medical and urologic consideration and adequate preoperative preparation is better than a skilful operation without preparation.

Ponce de Leon<sup>63</sup> favored deep roentgen-ray treatment in prostatic hypertrophy. He believed that if the prognosis is good, prostatectomy should be performed in every case. If the prognosis is poor, roentgen-ray treatment should be used. He does not limit roentgen ray to the treatment of hypertrophy, but cited four patients with chronic retention and vesical distention who were definitely benefited. He expressed the belief that radiocystitis will not result and that the blood urea content is not increased. Patients for roentgen-ray treatments must be as suitably prepared as for operation, so as to eliminate the possibility of uremia. Deep roentgen-ray treatment increases the difficulty of later enucleation. He felt that it does not enhance the change of adenoma to carcinoma (as believed by Legueu), and if all other specimens of operative cases were carefully sectioned, the same percentage of malignant lesions as found after radiation could be demonstrated.

Ponce de Leon reported a case of a patient, aged 74, whose preoperative diagnosis was adenoma. During the first operation, a hard knot was felt in the prostate gland and biopsy revealed adenocarcinoma. For this reason, and also because of the patient's poor health, deep roentgen-ray treatment was substituted for the second stage of prostatectomy with marked improvement. The author stated that had the roentgen ray been used first it would have been blamed for the carcinomatous change.

Ganissans<sup>64</sup> wished to refute Legueu and Compar, who in sixty cases of prostatic hypertrophy in which radiotherapy was used found only slight early decongestion. He stated that the latter is false, since, on the contrary, radiotherapy may start with congestion and edema

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63. Ponce de Leon, J.: Concepto urológico actual de la radioterapia profunda en el adenoma de la próstata (Replica). *Rev. méd. de Barcelona* 7:496, 1927.

64. Ganissans, Angel: La radioterapia en el adenoma prostático. *Rev. méd. de Barcelona* 7:483, 1927.

four near the right ureteral orifice, and one in the median line just behind the interureteric ligament. The size of the diverticula varied from 2.5 cm. in diameter to that of a normal bladder. The vesical walls were much thickened and hypertrophied. Marked inflammation of the mucosa of the bladder was present as a result of severe infection. The urine was foul and contained a large amount of mucus. The symptoms were dysuria and obstruction extending over periods of from four months to three years. Interval hematuria was the outstanding clinical feature. Frequency was present in all cases, and is probably accounted for by the infection and inflammation of the bladder. Retention occurred in several of the cases.

The diagnosis of this condition is impossible without cystoscopy. The symptoms do not distinguish it from prostatic obstruction and carcinoma of the bladder itself. A cystogram helps to make a diagnosis of diverticulum, but not of the indwelling tumor. The cystoscope may not even disclose the tumor unless it protrudes from the mouth of the diverticulum. Furthermore, the mouths of diverticula have peculiar sphincteric actions, so that unless the stoma of the diverticulum is observed at varying intervals or at different stages of the filling and emptying of the bladder, the condition might be easily overlooked.

The treatment has been for the most part an attempt at removal of the diverticulum. Targett gave the data from the necropsy in three of the ten cases here reported. In three cases reported by Judd and Scholl the diverticulum was excised, but in the fourth case the diverticulum was so adherent that excision was not attempted. Harris reported a case in which cystotomy was performed, but the extent of the growth prohibited resection. In Deming's case, resection was readily accomplished. Young reported the only cure in a case of a small diverticulum 2 cm. in width. The carcinoma was not infiltrating and had not metastasized at the time of operation.

Death occurred from twenty-five days to two years after operative procedures. According to Targett's report on three necropsies, infection, pyelonephritis and uremia were the immediate causes of death. Metastasis was noted in one of the cases reported by Judd and Scholl in the lymph nodes along the right internal iliac vessels, and in another case, there was a recurrence in the suprapubic wound after five months. In Deming's case, signs of local recurrence appeared between the bladder and the rectum eight weeks after excision; nodules in the liver were also found which were thought to be an extension of the process.

The carcinoma in Targett's case was epithelioma. In other cases, the growth was of a papillary nature. Microscopically, the section from Deming's case showed a tumor of a high degree of malignancy; the cells were angulated, reticular and contained many mitotic figures.

and therefore increase the difficulty which will subside after eight days and leave the patient improved. The cases indicated for radiotherapy are those of early prostatic hypertrophy with congestion, and chronic retention but without vesical distention, cases with only slight changes in the vesical neck and slight elongation of the prostatic urethra. The cases in which radiotherapy is contraindicated are those of chronic retention with vesical distention and marked changes in the neck of the bladder; these belong to the surgeon. Gamissans reported cases in which symptoms were not present for five years following treatment. He believed that radiotherapy does not increase the difficulty of enucleation any more than the duration of time in which other changes may take place. Finally, radiotherapy does not enhance the malignant degeneration of adenomas.

Thomas<sup>65</sup> outlined at length the various considerations that come into play in the management of prostatic lesions. The cystoscopic determination of the type of lesion, the amount of residual urine and the force with which the urine is expelled through the catheter, are all evaluated.

The estimation of the urea nitrogen of the blood and the excretion of phenolsulphonphthalein are the most commonly used tests of renal function by the majority of urologists. From 20 to 30 mg. of urea nitrogen in the blood are considered safe values, while values above 30 mg. for each 100 cc. are dangerous, if not prohibitive, for operation. Regarding the phenolsulphonphthalein output, definite values have not been determined. Thomas emphasized that an output of 10 per cent one week, 20 per cent the next, and 30 per cent the next is a better index for operative success than an output of 50 per cent one week and 35 per cent the next. An effort should be made to establish the stability of renal function. In cases with injury to the kidneys, reliance cannot be placed on a single test.

Thomas described what he has called the index of elimination. This index is computed by taking the ratio of the percentage output of the dye for the first and third cycles (twenty minutes each) of a one-hour period of major elimination. Normally, the ratio is 5:1 and the index is said to be 5. When the quantitative output for the first twenty-minute period is greater than, or at least equal to, that of the third period, retention of urea is not present and renal function is invariably demonstrated as excellent. Such cases are considered in the positive phase for operability. When the output for the first period is less than that for the third period, the index is obviously less than 1, the kidneys are injured and the patient is in the negative phase.

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65. Thomas, B. A.: *Vital Factors in the Management of Prostatic Obstruction*, Ann. Surg. 86:563, 1927.

rigid, a dead space is left on the side on which the operation was performed and thus exudation is induced, which may invite infection. In the experiments it was noticed that the less lung tissue removed the greater the chance for complete recovery. The method of leaving a certain amount of lung tissue to be used as a reinforcement over the bronchus is of distinct advantage. The danger of rupture in this stump is obviated first by the ligation of the larger bronchioles and also by the pneumothorax on the side on which the operation was performed. Another precaution is the production of temporary or permanent paralysis of the phrenic nerve at the end of the operation. This lessens the chance for an inspiratory suction action within the stump. If a stump of lung tissue is left, the pleural surfaces are approximated and thus a thick pleural covering is induced at the site of the resection of the lung. The fibrosis that occurs in the lung tissue of the stump adds to the efficiency of the operation.

In the operations in which the whole lung is removed and the bronchus is left exposed, none of the foregoing factors can be mobilized as aids. Moreover, the circulation, the vagus and the heart are disturbed by the unnecessary additional handling of the bronchus and its contiguous structures. Often it was found difficult to try such methods in ligating and suturing the bronchus without going through all its walls. Even with a perfect technic, the operation is much more prolonged than in the procedure employed in the present experiments. With the use of the technic described, it has been possible to complete the operation in from eight to twelve minutes from the time of the incision in the skin till the complete closure of the wounds. Our results with this type of operation are not different from those of Bettman.<sup>10</sup> The wall of the bronchus was found resistant, and the greatest difficulty has been in attempting to invert the stump.

#### CONCLUSIONS

The method described has been found satisfactory in experiments on the dog. It provides for a stump which eventually becomes strong and prevents any possibility of perforation of the bronchus. The method is simple, does not require any special instruments and can be finished in the shortest possible time. It provides for approximation of endothelial surfaces in a manner similar to operations on the gastro-intestinal tract or the blood vessels.

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10. Bettmann, R. B.: Experimental closure of Large Bronchi: A Study of the Factors Concerned in Failure of Bronchi to Heal, *Arch. Surg.* 8:418 (Jan.) 1924.

# ACUTE EMPYEMA

TREATMENT BY CONTINUOUS TIDAL IRRIGATION AND DRAINAGE  
DEPENDENT ON NORMAL RESPIRATORY MOVEMENTS \*

DERYL HART, M.D.

BALTIMORE

The closed method of drainage and irrigation of an empyema cavity offers many advantages, chief of which are: 1. The method is simple and easy of operation, the insertion of a tube through a trocar under local anesthesia requiring only a few minutes. 2. The pressure within the cavity can be released at any desired rate. 3. There is little care in the form of dressings. 4. The cavity is not continually sucking air. 5. So long as the junction of the tube with the wall of the chest is air tight, suction can be applied, thus reducing the pressure within the empyema cavity below the surrounding atmospheric pressure and thereby decreasing the size of the cavity by expanding the lung.

On the other hand, many arguments have been advanced against this method of treatment. The most important has been that the drainage is inadequate; the pus, which becomes thick, and fibrin collecting in the tube cause a damming up of the infected fluid within the chest. This results in an elevation of temperature, and necessitates the removal and reinsertion of the tube or considerable effort to dislodge the plug which causes the obstruction. Each blockage with a damming up of the pus delays convalescence, not only by the systemic effect of the absorption of toxins and bacteria, with the danger of septicemia and metastatic infection, but by the rapidly progressing positive pressure within the empyema cavity which delays the expansion of the lung, and at times goes so far as to increase the size of the cavity by pulmonary compression.

This positive pressure within the chest also causes the pus to dissect along the tube, which, in the absence of a bronchial fistula, is the only avenue of escape from the infected pleural cavity. The most favorable course is for the pus to reach the surface, soil the dressings and dissect from the wall of the chest the adhesive straps holding the tube in place. With the infection and sloughing of the tissues about the tube, it soon becomes so loose that the cavity can no longer be kept air tight; then one has none of the advantages of closed drainage, while the small opening is inadequate for open drainage. Only the unusual patient has gone for ten days to two weeks without having the tube changed or become loose, permitting air to leak in through the hole in the wall of the chest.

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\* From the Surgical Department of the Johns Hopkins University and Hospital.

By repeated determination and observation of such indexes of elimination, Thomas believed that an accurate estimate can be made of renal function in a much better manner than that offered by the usual method of total excretion.

In considering the cardiovascular system, Thomas noted particularly the blood pressure of his patients. In cases of low tension in which the systolic blood pressure is 110 or less, the diastolic must be more than 60. When the diastolic is less than 60, the systolic must be more than 110. In cases of high tension in which the systolic pressure is 180 or more, the diastolic must be less than 100; when the diastolic pressure is more than 100, the systolic must not be more than 175. It is emphasized that this is not alone pulse pressure in its usual sense, but rather pulse pressure with systolic and diastolic limitations.

The significance of the Wassermann test, the determination of the coagulation time of the blood and of the blood sugar are given appropriate attention. Anemia is frequently found and must be overcome in preoperative treatment. The nervous system comes in for consideration with the possibility of tabes, multiple sclerosis, etc., as complicating factors. Thomas reported cases in which the functional nervous disorder, uncontrollable fear of death, was an evil operative omen. Rarely will the pulmonary or gastro-intestinal symptoms present features which contraindicate operation, but usually any such symptoms may be overcome, especially if caudal and transsacral anesthesia are used. Age in itself is never prohibitive if the patient's organs can be brought to function properly.

Thomas favored suprapubic prostatectomy when the gland is greatly enlarged or when intravesical complications such as stone, diverticula, or trigonal hypertrophy exist. When the hypertrophy is confined to one or both lateral lobes or the gland is small, fibrotic and presumably adherent, undoubtedly it should be removed by the perineal route. Again, in the group of patients who have the bar or glandular type of obstruction, some form of punch operation or excision with the electric knife is indicated. Thomas advocated, in many such cases, the removal of orificial obstruction by means of the punch or rongeur, suprapubically, as it is more effective and thorough, and there is less danger from infection and hemorrhage than by the urethral route.

As indications for primary cystotomy and secondary prostatectomy rather than the one-stage operation after catheter drainage, Thomas named: (1) marked cystitis, (2) intravesical complication such as stone, tumor, clots, and so forth, (3) epididymitis, (4) stricture and some cases of false passage of the urethra, (5) unusually small or sensitive urethra, (6) unusually obstructive or impassable prostate and (7) febrile cases or catheter cases in which urethral fever and chill develop.

dissection along the innermost layer of tunic, infiltrating the lowest portion of the sac with anesthetic, if necessary to block the pudic nerves. The mass is then delivered through the wound and incised from end to end. The redundant tunica vaginalis is excised and complete hemostasis is obtained by a running suture in the tunica vaginalis if necessary. The remaining edges are everted and sutured behind the cord. Hemostasis is carefully watched and the testis is replaced in the scrotum. The wound is closed without drainage. A small gauze dressing and a special hemostatic bandage<sup>80</sup> are applied.

Complications, such as hemorrhage, infection, involvement of the testis, or recurrence of the condition, may ensue. Hematocele, if large, requires evacuation. Admonition as to the utmost care in asepsis is given. Scrotal edema may occur at times. Testicular involvement may be immediate in the form of traumatic orchitis or postoperative infection, and later there may be atrophy. In eight cases of this series, testicular involvement called for orchidectomy.

The average period in the hospital in this series was 9.3 days. Two patients died of bronchopneumonia following operations under local anesthesia.

Recurrence as quoted by Bruns was approximately 2.4 per cent. Campbell examined thirty-three cases of this series. In four a slight collection of fluid at the upper pole apart from the testis was noted. In two cases, there was definite recurrence. At the second operation it was found that two layers of the tunica vaginalis were glued together in the formation of a cyst, not involving the testicle but just above it.

[ED. NOTE.—This is an excellent review of a common and much neglected lesion. As Campbell pointed out, the procedure of choice is always open operation; recurrence of the condition is three times as severe after tapping and injection. The latter methods seem somewhat obsolete but it is sometimes necessary to consider them in individual cases.]

*Varicocele*.—Bate<sup>81</sup> reviewed the literature on varicocele carefully. Petit was the first to describe varicocele as one of the symptoms of renal tumor. In 1881, Guyon and Morris gave clear accounts of cases of this condition. Bate reported fourteen cases of varicocele and renal tumor from the records of the Massachusetts General Hospital. From these he found that varicocele is a late sign and carries with it a poor prognosis. Only 28 per cent of his patients were temporarily relieved by operation. The condition is probably not often noted in early

<sup>80</sup>. For description of this unique bandage reference is made to the original article (footnote 79).

<sup>81</sup>. Bate, J.: Symptomatic Varicocele, J. Urol. 18:649, 1927.

For an anesthetic, much depends on the case. An absolute rule is not given. In certain cardiovascular, renal and pulmonary cases spinal, regional, or other forms of local anesthesia, unquestionably should be used. Most patients, if properly prepared, stand general anesthesia under gas or even ether well, much depending on the efficiency of the anesthetist.

Hemostasis is satisfactorily obtained with suture of the bleeding points at the time of operation. The use of the pneumatic bags of Hagner, Pilcher or Ballenger is advocated; packing of the prostatic fossa is the least desirable method.

Ligation of the vas as a preventive of epididymitis is regarded as unnecessary in most cases. Suction drainage is not used.

Postoperative care is held in equal importance with preoperative treatment. Sodium chloride and dextrose solutions, diuretics and cardiac tonics, especially digitalization, save many lives. The importance of vesical irrigations in the presence of infection and of general hygiene of the bladder in the prevention of pyelitis and pyelonephritis is emphasized. These old men should not be forced out of bed too soon. Many complications of epididymitis and a few of phlebitis and embolism will thereby be avoided.

[ED. NOTE.—While there are details with which some may disagree, Thomas has reviewed many features of handling prostatism which show experience and sound judgment. His description of the value of determining an index of elimination, his evaluation of blood pressure readings and his indications for the two-stage procedure are particularly appealing and seem worthy of practicing. It is to the credit of urology as a specialty that a low operative mortality has been achieved in what appears to be and has been the poorest sort of surgical risk. The low mortality rate has been the result of the many improvements in operative technic and the conscientious and detailed physiologic and biochemic studies during the periods preceding and following operation.]

Lowsley and Harrah<sup>66</sup> reported the unusual case of a man, aged 32, who had had urinary obstruction due to prostatic tumor for three months and was admitted to the hospital with complete urinary retention. Catheter drainage and preliminary care were followed by cystoscopy, which revealed enlargement of the prostate. Suprapubic cystostomy was performed at which time a piece of the tumor was removed for examination. Fourteen days later, the prostate was

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66. Lowsley, O. S., and Harrah, F. W.: Enlargement of the Prostate Gland with Characteristics Resembling Hodgkin's Disease: Malignant Granuloma, *Ann. Surg.* 86:556, 1927.



examinations because the patient is examined while recumbent. Thrombosis and tumor in the left renal vein occur with and without varicocele and are probably significant etiologic factors. Enlarged lymph nodes were recorded in one of the cases in which operation was performed. Pressure from the tumor would account for the varicocele in several cases.

Although many writers refer to varicocele as a symptom of lesions other than malignant tumor, the records of the Massachusetts General Hospital do not bear this out. One case was reported from the literature, in which varicocele occurred with severe pyonephrosis. Although symptomatic varicocele is a late sequel and carries with it a poor prognosis, in properly selected cases the chance for temporary relief should not be denied the patient merely because symptomatic varicocele is present. When a suddenly developing varicocele is noted in a patient of advanced age, renal tumor should be considered. Varicocele occurred in 20 per cent of the cases of hypernephroma and in 11 per cent of all malignant tumors of the kidney; it was the presenting symptom in 30 per cent of Bate's cases.

*Epididymitis.*—Wade,<sup>82</sup> in discussing treatment, divided vaso-epididymitis into five stages according to clinical symptoms and pathologic manifestations.

In the first stage the patient usually presents himself complaining of pain in the groin and along the course of the vas deferens; there is a general feeling of malaise, which indicates that vasitis is present and the descending infection will soon involve the epididymis. The patient is immediately put to bed without further local treatment to the urethra or prostate, ice is applied to the painful area and 15 grains (0.972 Gm.) of calcium chloride is administered intravenously. This is repeated daily until the pain disappears. At this stage, a vas puncture with injection of the seminal vesicle on the affected side can be done satisfactorily. This is an attempt at abortive treatment.

The second stage is that in which the epididymis has become involved; there is slight swelling, tenderness and pain along the course of the vas deferens, and general malaise. Such patients also are sent to bed; calcium chloride is given daily intravenously; the scrotum is elevated and cold applications are applied. Diathermy may be used to good advantage. The epididymitis may subside at this stage or it may pass into the third stage.

In the third stage, there is considerable enlargement of the epididymis and all the symptoms are much more severe than in the previous stage. In some of these cases Wade expressed the belief

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82. Wade, H. K.: Treatment of Acute Gonorrheal Epididymitis with Special Attention to Prevention of Azoospermia, *J. Urol.* 18:427, 1927.

removed under regional anesthesia. At one point the prostate had infiltrated the prostatic capsule and malignancy was suspected. Microscopic examination of the growth showed newly formed granulomatous tissue, rich in plasma cells and containing mononuclear giant cells suggestive of the Sternberg type, and eosinophilic leukocytes. An inguinal lymph node, removed for section, showed simple chronic lymphadenitis.

The microscopic picture suggested a granuloma of the type of Hodgkin's disease and relative lymphocytosis. However, other features of Hodgkin's disease, which are carefully outlined by the authors, were wanting.

The unusual condition of complete urinary retention due to solid prostatic tumor in a patient, aged 32, is emphasized; a case of the kind had not been reported previously. The gradual onset of symptoms exhibited by the patient is similar to those described in most cases of adenomatous enlargements of the prostate in old men. The usual and frequent painful urination culminated in complete retention of urine rather more rapidly than in most cases of adenoma.

[ED. NOTE.—The histologic picture presented is even more uncommon than the rarity of prostatic obstruction in early adult life. Sarcoma of the prostate occurs much earlier and cancerous neoplasm much later than the age of 32. Furthermore, Hodgkin's disease rarely affects the prostate. Tuberculosis, a condition at times confused with Hodgkin's lymphadenitis, was considered but none of the features of tuberculosis was present. Unfortunately, the follow-up record of the patient is not mentioned. This might reveal further interesting information in this most rare clinical and pathologic picture.]

Leguen<sup>67</sup> reported a number of cases of hypertrophy of the vesical neck. The hypertrophy involved not only the fibromuscular and glandular tissue, but also all the other tissues which comprise the vesical neck. Usually symptoms of retention are present over a long period. Leguen considered the glandular hypertrophy as a mild type of prostatic disease. In prostatic disease various types of adenoma may be found. There may be adenomas which weigh only a few grams, some that are barely perceptible to the eye and others so small that only the microscope can establish their existence. Functional symptoms are more marked and appear earlier in fibromuscular hypertrophy than in glandular hypertrophy. At times these hypertrophied areas contain histologic signs of secondary infection. Excision of the neck of the bladder is the best treatment for this condition.

<sup>67</sup> Leguen: L'hypertrophie du col vésical, Bull. Soc. franç. d'urol. 6:222, 1927.

that he is justified in prescribing rest and using the expectant treatment outlined, but in many cases the Hagner operation should be performed.

In the fourth stage, the epididymis is enormously enlarged with more or less severe orchitis and hydrocele. The temperature is elevated and leukocytosis is marked. The patient is toxic and suffers intensely. In all such cases, the radical or surgical method should be carried out early.

Azoospermia can be prevented in a large percentage of cases by a carefully performed epididymotomy in selected cases.

Gurewitsch<sup>83</sup> discussed two cases of gonorrheal funiculitis. Clinically, the symptoms were peritoneal and suggested the diagnosis of strangulated hernia. In both cases the aponeurosis was split down to its lowermost layer to obviate any stasis, and the entire funiculus freed in layers. Closure was then carefully made, and healing occurred in eight days. Hernias did not result. According to Gurewitsch, operation hastened healing.

*Urogenital Tuberculosis.*—Marion<sup>84</sup> has performed 1,267 operations for genital tuberculosis since 1908. He has found the testis affected in about a tenth of these cases. In the remainder, the infection was localized to the epididymis.

Epididymectomy, which is more difficult to perform than nephrectomy, is possible even in advanced cases. In order to prevent the formation of fistula, Marion divides the vas and fixes it to the skin. The wound is left partly open. Cicatrization usually proceeds rapidly. He considers general postoperative treatment, such as good air, sunlight and ultraviolet lights, important. He also uses so-called antigen of Negre and Bouquet (apparently a tuberculin treatment), prepared at the Pasteur Institute. Castration is performed only as a last resort.

Wildbolz,<sup>85</sup> in discussing the treatment of urogenital tuberculosis, stated that he has obtained satisfactory results by epididymectomy combined with general postoperative treatment. More than 60 per cent of his patients were definitely cured, while 20 per cent died of pulmonary, renal, or other forms of tuberculosis. In order to save the testis, Wildbolz recommended early epididymectomy as the treatment of choice in cases of acute epididymitis.

Choltsoff<sup>86</sup> stated that tuberculosis of the prostate and vesicles usually accompanies tuberculosis of the epididymis. Isolated tuber-

83. Gurewitsch, G. M.: Zur chirurgischen Behandlung gonorrhöischer Funiculitiden, *Zentralbl. f. Chir.* 54:1225, 1927.

84. Marion: Traitement de la tuberculose génitale chez l'homme, *J. d'uro.* 24: 358, 1927.

85. Wildbolz: Traitement de la tuberculose génitale chez l'homme, *J. d'uro.* 24:357, 1927.

86. Choltsoff: Tuberculose uro-génitale, *J. d'uro.* 24:464, 1927.

Kreutzmann<sup>68</sup> noted that although hydro-ureter and hydronephrosis have long been associated with obstructive urethral lesions the mechanism of formation of the dilatations is still an open question. His investigations have demonstrated that ureteral reflux is not common in obstructive lesions of the vesical neck and urethra. Reflux usually is unilateral and dilatation of the ureter and renal pelvis has even been demonstrated on the intact side.

Kreutzmann expressed the opinion that his investigations tend to substantiate Tandler and Zuckerhandl's theory that the dilatation of the upper part of the urinary tract is due to the vas deferens. Kreutzmann concluded that (1) in cases of hypertrophied prostates, hydro-ureter and hydronephrosis may occasionally occur as a result of the kinking of the ureters by the vas deferens; (2) the most common cause of dilatation of the upper part of the urinary tract in obstructive lesions of the vesical neck and urethra in adults is constriction of the intramural portion of the ureter; (3) this constriction is due to hypertrophy of the musculature of the bladder surrounding the ureters; (4) reflux is not common in these conditions, and when present, it is caused by an infection in the ureter resulting in a stiffening of its intramural portion, and (5) reflux is a terminal and not a primary phenomenon of prostatic hypertrophy and urethral stricture.

Alyea<sup>69</sup> pointed out the high incidence of epididymitis in cases of prostatic obstruction. This incidence is reported by White of London as 82 per cent, which is an unusually high percentage as White included many cases of slight induration as true epididymitis. From other reports, it would appear that about 40 per cent is a correct estimate of the occurrence of this complication.

Alyea pointed out the practical importance of preventing both preoperative and postoperative epididymitis in cases of prostatic obstruction. Statistics from various clinics emphasize the far too frequent occurrence of this complication. The advance in methods for its prevention was traced through seminal vesiculectomy, ligation of the ejaculatory ducts, to ligation of the vas in the scrotum by a closed method. It is demonstrated that the time for ligating is not at the operating table after the patient has already been handicapped by present or latent epididymitis, but at the time of his admission to the hospital, before urethral instrumentation or the insertion of a retention catheter. This is strongly advised for adoption as a ward routine in all cases of prostatic obstruction. To make this practicable, he has

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68. Kreutzmann, H. A. R.: The Cause of Renal Back-Pressure in Obstructive Lesions of the Urethra and Bladder Neck, *J. Urol.* 19:199, 1928.

69. Alyea, E. P.: Vaso-Ligation a Preventive of Epididymitis Before and After Prostatectomy, *J. Urol.* 19:65, 1928.

culosis of the prostate might sometimes occur, but isolated tuberculosis of the vesicles is never seen. Epididymectomy is indicated in advanced cases or in cases in which the disease is progressing rapidly. If a portion of the testis is also infected, this part should be removed. Epididymectomy and orchidectomy favorably influence prostatovesicular tuberculosis. In advanced cases, it is necessary completely or partially to remove these organs. The perineal route is usually the more desirable one.

Abricosoff<sup>87</sup> stated that in the majority of cases tuberculosis of the urogenital system develops from hematogenous metastasis from a primary pulmonary focus.

#### URETHRA

*Tumors.*—Wurmser<sup>88</sup> stated that carcinoma of the urethra is observed in the perineoscrotal, penile and balanic urethra in decreasing frequency. Two significant elements in the etiology seem to be chronic gonorrhea and the transformation of urethral polyps. Carcinoma of the glands and of the balanic urethra both develop from squamous epithelium. In the deep urethra the cells are of the cylindric type. Metastasis is common, especially to the lungs. Disturbances of micturition are usually the first symptoms; others are tumor, pain, hematuria, discharge, fistulas and adenopathy. The diagnosis and differential diagnosis are thoroughly discussed. Death in from six months to one year is the usual result in untreated cases.

[ED. NOTE.—Usually carcinomas in the posterior urethra of the male, although developing on a cell that is somewhat cylindric, infrequently have squamous cell characteristics. Some of the cases reported by Wurmser were of short duration and death occurred shortly after the first appearance of trouble. In several cases reported by other observers, the appearance of the carcinoma was preceded by long periods of urinary difficulty and irritation. The tumor formation is somewhat analogous to the long standing premalignant stages preceding the development of squamous-cell tumors of the urinary bladder. Konig reported a case of urethral carcinoma developing after urinary obstruction of forty-eight years' duration, and Oberlander noted a somewhat similar case developing after forty years of urinary difficulty. Infection is unquestionably an important factor in the formation of these urethral growths. Infection usually progresses to the point of stricture and the malignant changes come later. Traumatic strictures also have the same malignant potentialities as those of infectious origin. The majority

87. Abricosoff: Tuberculose uro-génitale, *J. d'urol.* 24:463, 1927.

88. Wurmser, Raymond: L'épithélioma primitif de l'urètre périnéal chez l'homme, *J. d'urol.* 24:497, 1927.

described in detail the technic of vasoligation through the skin, without an anesthetic, which is done in bed or in the ward treatment room. At the Brady Urologic Institute, the vas has been ligated in fifty cases of prostatectomy<sup>70</sup> according to the procedure, and the percentage of occurrence of epididymitis is four. They believe, therefore, that if this regimen is adhered to rigidly the occurrence of preoperative as well as postoperative epididymitis in the treatment of prostatic obstruction can be practically eliminated.

[ED. NOTE.—Many urologists are now employing some type of vasoligation as a routine. If done early enough, this simple procedure usually prevents epididymitis and in some cases it may save life.]

Scott<sup>70</sup> reviewed the dangers of rapidly emptying the chronically overdistended bladder and the various methods of decompressing such bladders more slowly. According to his observations, the best results are obtained by taking a relatively short time to empty the bladder, namely, about twenty-four hours. To accomplish this, he has successfully used an ordinary olive-tipped ureteral catheter. Decompression by means of a ureteral catheter has been used only as an emergency measure in his clinic. It has been of special value in those cases of carcinoma of the prostate in which the lumen of the prostatic urethra was so markedly decreased in size that it was impossible to pass anything larger than a filiform. In such cases the ureteral catheter also acts as a dilator, and it is possible, by inserting larger catheters every two days, to dilate the urethra rapidly so that a soft rubber catheter can be passed within a short time. The method also proved to be satisfactory in the case of a small boy having acute paradoxical incontinence due to the presence of a congenital urethral valve.

Because of the satisfactory results obtained by the apparatus now in use for decompressing the bladder in the presence of retention due to simple benign prostatic hypertrophy, the ureteral catheter has not been used in such cases. However, there does not seem to be any good reason why this method could not be used if decompression of the bladder is otherwise impossible.

*Tuberculosis.*—Bothe,<sup>71</sup> in searching the literature, found only nine cases of tuberculosis of the prostate gland without demonstrable coincident tuberculosis elsewhere in the genito-urinary tract, and to these he added a tenth case. In four of the cases, the prostate had undergone hypertrophy. His case presented the usual signs and symptoms of benign adenomatous hypertrophy of the prostate. Pros-

70. Scott, W. W.: Gradual Decompression of the Bladder with a Ureteral Catheter. *J. Urol.* 19:81, 1928.

71. Bothe, A. E.: Primary Tuberculosis of the Prostate, *J. Urol.* 18:494, 1927.

of carcinomas which follow long standing infection and trauma occur in men of the cancer age and commonly occur at the usual site of stricture formation in the cavernous and membranous urethra. Occasionally they occur in the penile urethra, but rarely in the fossa navicularis. Of forty-two cases of carcinoma of the male urethra reviewed by Preiswerk, thirty-eight were in the membranous or cavernous urethra. Wurmser stated that metastatic growths are common, but it has been the experience of other observers that metastasis only occurs in the later stages. When secondary deposits occur they have the same tendency to remain localized in the primary glands as do those arising from epitheliomas of the penis. In young men, carcinoma is more likely to be papillary than squamous cell, and the long premalignant period of trauma and infection is generally absent. Papillary carcinomas in most reported cases were extremely malignant; they rapidly infiltrate the surrounding tissues and metastasize freely. Hutchison reported a case of a man, aged 22, with papillary carcinoma of the urethra; ulceration through the body of the penis occurred three weeks after the onset of swelling and obstruction. Six weeks after the first symptoms the regional glands were involved.]

*Epispadias.*—Sexton<sup>89</sup> stated that epispadias in women rarely occurs. Lower noted only forty-three cases in the literature up to 1922. He added one to the number. Sexton reported the case of a woman, aged 27, with marked separation of the labia minora and labia majora, rudimentary clitoris, an intact urethral sphincter and diastasis of the symphysis, but not associated with incontinence. Treatment was not attempted.

*Priapism.*—McKay and Colston<sup>90</sup> stated that true persistent priapism is rarely noted. Hinman had reviewed 170 cases up to 1914. They searched the literature carefully and found 22 others, making the total 192 cases. It was noted that if the erection persists for two days or more thrombosis is present in the corpora which in itself is sufficient to sustain the erection. Hence, if the underlying cause is treated successfully the erection will persist until the clot in the corpora is disposed of either by absorption or by evacuation. The immediate relief of the patient's symptoms depends on the collapsing of the penis by emptying it of this clot. It is, therefore, advocated that the erection be first relieved and the etiologic factor treated later. Various medical measures have been utilized. The use of sedatives, narcotics and hypnotics are usually of no avail. Deep anesthesia has been tried, and spinal

<sup>89</sup> Sexton, W. G.: Epispadias in Women: Case Report, J. Urol. 18:663, 1927.

<sup>90</sup> McKay, R. W., and Colston, J. A. C.: Priapism: New Method of Treatment, J. Urol. 19:121, 1928.

tatectomy was performed. On microscopic examination of the removed gland, a tuberculous focus was found. Other evidence of tuberculosis was not found. Tuberculosis of the genito-urinary tract forms about 5 per cent of all tuberculous cases found at necropsy and evidence of pulmonary tuberculosis is frequently found associated with genito-urinary tuberculosis. The prostate is frequently the seat of an associated tuberculous lesion when the other genito-urinary organs are primarily infected, but tuberculosis of the prostate, as a primary lesion in genito-urinary tuberculosis, is exceedingly rare. Hypertrophy may follow a tuberculous lesion of this gland.

[ED. NOTE.—Primary tuberculosis of the prostate is a rare condition. Grossly, it sometimes resembles carcinoma, particularly after the specimen has been removed, hardened and sectioned. Clinically, other symptoms of urinary infection usually distinguish this condition from malignancy. With secondary tuberculosis, the prostate usually becomes hard, small, fibrous and slightly nodular.]

*Prostatic Secretion.*—McCarthy<sup>72</sup> and his associates reported data regarding the chemical composition of the prostaticovesical secretions of normal young men. These secretions contain an unusually high concentration of calcium, inorganic phosphorus, "hydrolyzable" phosphorus and amino nitrogen. It is believed that the amino nitrogen and hydrolyzable phosphorus may be partly in the form of spermin.

The sugar concentration showed marked variations. The sugar content of fresh semen greatly exceeded that of blood. Glycolysis was observed during incubation of the semen at 38 C. for from nine to twelve hours. The decrease in sugar was accompanied by a rise in lactic acid. However, the amount of lactic acid formed does not account for all of the sugar lost. It is probable that glycolysis is a phenomenon attributable to living spermatozoa, and that the lactic acid is an intermediate product in the utilization of sugar.

A study of the hydrogen-ion concentration of the semen during glycolysis demonstrated an efficient buffer mechanism in this fluid.

#### TESTIS AND EPIDIDYMIS

*Tumors of Testis.*—Morris<sup>73</sup> gave a general discussion of the present status of the theories and classification of testicular tumor. Ewing stated that all tumors are teratomas; Chevassu maintained that there are two classes of testicular neoplasms differing essentially in cell mor-

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72. McCarthy, J. F.; Stepita, C. T.; Johnston, M. B., and Killian, J. A.: *Biochemical Studies of Prostato-Vesicular Secretions*, J. Urol. 19:43, 1928.

73. Morris, J. H.: *Malignant Tumors of the Testicle with Special Reference to Classification*, Arch. Surg. 15:530 (Oct.) 1927.



anesthesia in early cases. The latter should be effective provided thrombosis has not set in.

Surgical treatment is carried out as follows: (1) radical amputation if the erection is sustained by the presence of a local malignant neoplasm; (2) ligation of the dorsal arteries; (3) division of the ischiocavernosus muscles in the perineum and the arteries and nerves that pass through them, and (4) incision into the corpus cavernosum and evacuation of the contents of both sides.

McKay and Colston reported three cases with favorable results. They advocated and used the method of aspiration of the corpora, under local anesthesia. This procedure can be repeated several times if priapism returns.

McKay and Colston concluded that the easiest method of evacuating the blood clot in the corpora is by aspiration. It may be done with minimal danger. There are no contraindications to its frequent employment if necessary. The method of aspiration produces much less trauma to neurovascular mechanism producing erection than more radical surgical procedures, thereby enhancing the probability of subsequent normal erections.

phology and histogenesis: (1) embryonal, distinguished by their heterologous, atypical structure and embryonal origin, and (2) the simple, homologous, unicellular growths arising from fully differentiated adult tissues. Because of the controversial nature of the field, a case was reported which was of especial interest since embryonal adenocarcinoma and seminomatous tissue were found coexisting. Morris, therefore, concluded that: (1) the large cell tumor of the testis is of the embryonal type, (2) the theory of invariable unicellular or homologous nature is herein disproved and (3) the evidence adduced from this case substantiates Ewing's theory of teratomatous origin.

[Ed. NOTE.—The evidence is slowly gathering in favor of Ewing's theory of the teratomatous origin of malignant testicular tumors. Universal acceptance of this theory would tend to end the confusion which characterizes the classification. Although the classification of testicular tumors has been greatly simplified through the classic investigations of Wilms, Ewing and others, two opposing schools have arisen, one maintaining that "for practical purposes there exists only tumor of the testis, namely, a teratoma" (Ewing, O'Crowley and Martland, Wilms, Pick, Ribbert) and the other, that besides the teratomatous group, there is a large proportion of testicular neoplasms which are purely homologous or single cell tumors (seminomas) derived from the cells of the spermatic tubules (Chevassu, Frank, Schultz and Eisendrath, Sakaguchi, Vecchi, Geist and Thalheimer, Hardonia and Patel). The recording of such reports as those of Morris and Hinman, Gibson and Kutzmann will in time effect a reconciliation of these opposing schools and eradicate much of the confusion in their classifications. The teratoma of the testis is a tumor of tridermal origin, and the unicellular type of tumor, such as the seminoma, can be considered an overdevelopment of one tissue in a tridermal growth. Hence the term "teratoma testis" should be used inclusively, and, as such, signify all types of degeneration. It is well to remember that in general the malignant elements in mixed tumors are almost uniformly epithelial and therefore carcinomatous in nature, and that these carcinomatous elements in the teratoma are generally amenable to classification into one or more of three groups: (1) trophoblastic (chorio-epithelioma), (2) hypoblastic (adenomatous type), and (3) epiblastic (solid alveoli of basal cell type and tumors of the neurocytoma group)].

Proust<sup>74</sup> reported two cases of seminomatous tumors of the testicle observed by Proust and Mallet in 1922, in which rapid absorption was obtained with hard roentgen rays. In the first case there was a swelling

74. Proust, R.: État actuel de la radiothérapie des séminomes, *Bull. de l'Assn. franç. p. l'étude du cancer* 16:247, 1927.

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of the right leg, which was believed to be phlebitis, but which disappeared rapidly following radiotherapy. Since there have been similar cases, Proust assumed that the condition was due to obstruction of the lymph channels by carcinoma cells. In order to prevent the obstruction of the lymph channels and the formation of metastasis, soft rays were used which minimize roentgen-ray burns. In six cases of seminoma, the duration of life was lengthened fourteen, nineteen, thirteen and twelve months, and two patients are alive two and three years respectively since beginning treatment.

Pearlman<sup>75</sup> reported a case of torsion of an undescended abdominal testicle associated with malignancy. In patients, aged 18, undescended testicles are doubtless more prone to malignant change and torsion than are normally placed testes. Pearlman's case is of interest in that both conditions are seen in the one case.

Valdoni<sup>76</sup> stated that tumors of the genitals range as follows in the order of frequency: testis, epididymis, vas deferens, seminal vesicles and tunica vaginalis. He described a case of a small cell sarcoma of the dividing membrane of the scrotum in a boy, aged 17, which developed one and a half years after the scrotum had been injured by a hoof. Castration with complete extirpation of glands to the renal hilum was carried out. Metastasis occurred shortly afterward.

Chwalla<sup>77</sup> stated that sarcomas are the most common of tumors of the spermatic cord and lipomas are next in frequency. The literature, mostly French, reports about twenty-four cases. Chwalla reported a case of fibrosarcoma of the spermatic cord. The tumor was a rapidly growing spindle cell fibrosarcoma with giant cells and apparently originated either from the tunica vaginalis or the connective tissue between the cremasteric fibers.

*Diagnostic Aspiration.*—Huhner<sup>78</sup> reiterated his advocacy of aspiration of the testis as a prognostic and diagnostic procedure in sterility. He expressed the belief that operation should not be undertaken for relief of obstructive sterility without first aspirating the testis, to ascertain whether or not spermatozoa are present.

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75. Pearlman, S. J.: Malignancy in an Undescended Abdominal Testis with Torsion, *J. Urol.* 18:637, 1927.

76. Valdoni, P.: Sarcoma primitivo della vaginale de testicolo, *Policlinico* 34: 244, 1927.

77. Chwalla, Rudolf: Ein Fall von Fibrosarkom des Samenstranges, *Ztschr. f. urol. Chir.* 23:419, 1927.

78. Huhner, Max: Aspiration of the Testicle in the Diagnosis and Prognosis of Sterility, *J. Urol.* 19:31, 1928.

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*Hydrocele.*—Campbell<sup>79</sup> analyzed 502 cases of hydrocele observed at the Bellevue Hospital. He pointed out that hydrocele in infants is rare, practically always congenital and associated with hernia. Ninety per cent of the patients were more than 21 years of age; 27 per cent were between 20 and 30. The right side is slightly more often affected than the left. Bilateral hydrocele was noted in four cases. The shortest duration was three days, and the longest sixty years. In more than 50 per cent of cases, the duration was between two months and three years.

Inflammation in the form of epididymitis is probably the most frequent precursor of acute or chronic hydrocele. This is most frequently gonorrheal; it may be tuberculous, and at times nonspecific. Careful examination of the exposed epididymis will in most cases reveal a pathologic organ showing the postinflammatory changes of hypertrophy or atrophy. Occasionally, hydrocele follows or accompanies orchitis. One patient had mumps immediately preceding the appearance of the hydrocele. Trauma may be and not infrequently is an etiologic factor. Thirty-four patients of this series noted an actual blow to the testis preceding onset of swelling. Campbell pointed out that operative trauma in the region of the spermatic cord, such as herniotomy entails, may cause hydrocele, and warned against undue injury to the vaginalis and testis during such procedures. Congenital hydroceles in adults are rare since the condition, if present, usually disappears spontaneously in infancy. The majority fall into the idiopathic group, but Campbell believes that unrecognized asymptomatic epididymitis is again the usual underlying process.

Pathologically, the fluid of uninfected hydroceles resembles blood serum, has a specific gravity of 1.020 to 1.026, and contains fibrin, albumin, paraglobulin, and at times cholesterolin and phosphatic calculi. Microscopically, endothelial cells, cholesterolin crystals, leukocytes, often spermatozoa, bacteria in infected cases, and in the event of hemorrhage, erythrocytes are shown. Caforio is quoted as stating that in view of the lower specific gravity and smaller serum content of transudates, fluid in the hydrocele is an exudate of inflammatory origin.

Symptomatically, if hydrocele is acute and the result of inflammation of the epididymis or testis (rarely trauma), pain is likely to be severe. Pain is usually proportionate to tension, severe with rapidly forming hydrocele accompanying acute gonorrheal epididymitis, and slight or absent with hydrocele and tuberculous epididymitis. Chronic hydrocele, uncomplicated by infection, is usually without symptoms save for

<sup>79</sup> Campbell, M. F.: Hydrocele of the Tunica Vaginalis: Study of 502 Cases, *Surg. Gynec. Obst.* 45:192, 1927.

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[illegible]

swelling. Some patients complain of a dragging sensation in the scrotum or along the cord due to the weight of the mass.

In cases of hydrocele of the tunica vaginalis, inspection reveals a pear-shaped tumor tapering into the cord. As a rule the outline is felt to be smooth and regular and the mass elastic. Occasionally, lobulation is noted. The mass is dull to percussion, transmits light, cannot be reduced (except the congenital type), and unless complicated by hernia, does not give impulse. The cord is normal unless involved in the hydrocele. The scrotal skin may be tense and shiny over acute hydroceles and over chronic large hydroceles. Usually testitis occurs behind and below the center of the tumor; rarely is it anterior and often it cannot be localized. Although puncture and withdrawal of the fluid is the surest diagnostic procedure, it should never be used unless hernia can be ruled out absolutely.

In the differential diagnosis, hernia, spermatocele, hematocele, chylocele, gumma, edema of chronic passive congestion and testicular neoplasm are considered.

Tapping or the use of a local irritant, such as painting the overlying skin with tincture of iodine, frequently accomplishes cure in infants; sometimes cure is spontaneous. In adults, spontaneous cure is never obtained. Internal medication is of no value. Tapping with or without injection and open operation are employed now in treatment. Tapping is often curative in cases of children and may be used for adults if they refuse operation and for those whose physical condition does not warrant operation. Injection of from 5 to 20 minims (0.3 to 1.25 cc.) of pure phenol after completely emptying the sac, with kneading of the scrotum to disseminate the drug to all surfaces, may be employed in uncomplicated hydroceles with thin walls and clear fluid. It should not be employed for children if it cannot be determined whether or not the sac communicates with the abdominal cavity; if it does, fluid will reform.

Open operation is the treatment of choice. Simple eversion (the bottle operation of Andrew) is useful for small hydroceles without thickened sacs. Volkmann incised the sac widely and swabbed the cavity with phenol. Convalescence is slow and the percentage of recurrences high. Campbell prefers the excision and eversion operation of Winkelman. Cutaneous and deep injections of procaine for anesthesia are made, the cord is isolated and thoroughly infiltrated, thus affording complete testicular block. By carefully incising the parietal tunica until the innermost layer presents a bluish hue, much hemorrhage may be prevented in later dissection. If the hydrocele is unusually large, most of the fluid is withdrawn before the sac is incised. With hydroceles of ordinary size, the practice is to mobilize the unopened sac by blunt



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The more unfavorable complication has been for the pus to reach the subcutaneous tissues and to dissect beneath the skin, at times causing an infection more serious than the empyema, and necessitating multiple incisions; occasionally, if not recognized early, it has led to a fatal termination. This danger is greatest when the hemolytic streptococcus is the organism that causes the empyema.

In the class of minor disadvantages may be placed the presence of thick pus, which makes the irrigation of the cavity slow and difficult; the tendency, as healing progresses, to overdistend the cavity which is tending to collapse; the leakage of pus around the tube, demanding frequent dressings; and the plugging of the tube, causing almost continuous irritation and annoyance to every one concerned in the care of the patient.

In considering various methods to overcome these difficulties, it was thought that the natural movements of the chest with their pumping action could be utilized to give a continuous irrigation, and at the same time avoid the possibility of forcing in fluid under pressure. The original plan was to use an inflow and an outflow tube, each equipped with valves. It was found, however, that a simple tidal flow through as short a tube as possible was entirely satisfactory and gave the least possibility of becoming obstructed. With a continuous flow in one direction, fibrin blocks the opening to the outlet tube, but with the tidal flow it becomes dislodged at the next inspiration when the fluid flows into the chest.

The irrigation apparatus shown in figure 1 was soon adopted. This consists of a rubber tube which is passed into the dependent part of the empyema cavity through a trocar thoracotomy wound, and just outside the chest is connected by means of a T tube with a rubber bag on one side and on the other with a rubber tube leading through a Y tube to an irrigation bottle above and a drainage bottle below. The rubber bag is strapped to the abdomen just below the trocar thoracotomy wound, placing it slightly below the level of the empyema cavity with the patient in Fowler's position. This gives a slight amount of suction at all times. Since the entire system is closed, it is impossible for air to enter if fluid is kept in the irrigation flask and the drainage tube is always, when unclamped, below the level of the solution in the drainage bottle. This statement presupposes that the empyema is not complicated by a bronchial fistula, and that the tube fits snugly within the opening through the wall of the chest. The bag can be entirely emptied and suction applied to the empyema cavity by removal of the clamp to the drainage bottle. When this condition has been maintained for the desired length of time and the bag is partially refilled, there is no possibility of causing a positive pressure within the empyema cavity. The bag is never completely distended and usually is only from one-fourth to one-half full.

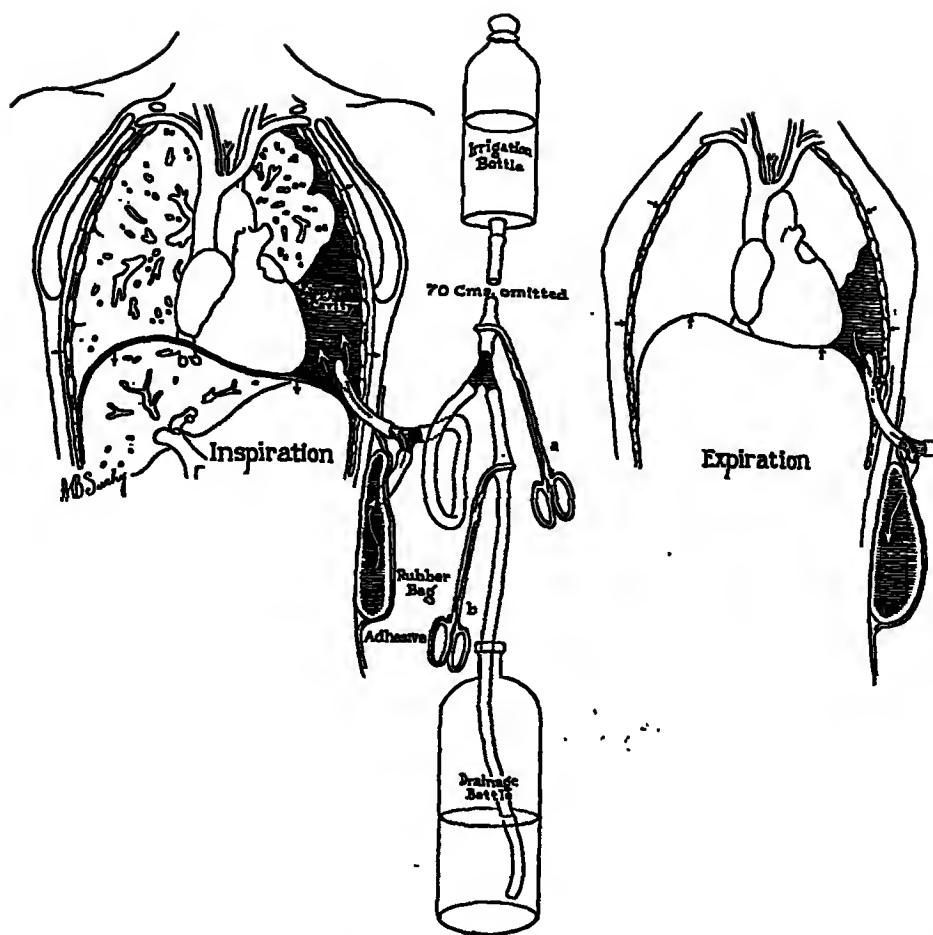


Fig. 1.—Diagrammatic illustration of the apparatus connected with the empyema cavity as shown in a cross-section of the chest. On the left is illustrated the effect of inspiration with enlargement of the thoracic cavity, and the reduction of the intrathoracic pressure below the surrounding atmospheric pressure. Thus the atmospheric pressure forces the fluid within the rubber bag strapped to the abdomen into the empyema cavity. With expiration, illustrated on the right, the intrathoracic space is passively or forcibly compressed with the outflow of air from the lungs and also of fluid from the empyema cavity, resulting in a diminution in the size of the cavity. This continues with each respiration, the consistency of the fluid within the empyema cavity and the rubber bag gradually approaching a common level. Before this is reached, however, clamp *b* is removed, the rubber bag is completely emptied, as much fluid as possible is siphoned from the empyema cavity, clamp *b* is reapplied, and clamp *a* is removed until the desired quantity of clean solution has flowed into the rubber bag and empyema cavity. The gradual mixing by means of the tidal flow again begins, and thus the consistency of the fluid within the empyema cavity gradually approaches that of the irrigating solution, the final point of dilution being determined by the amount of irrigation fluid kept in the bag, the frequency of its replacement, and the division of the time between irrigation and suction.



cavity, and with the patient in Fowler's position, there is always a slight amount of suction, but not enough to prevent a free tidal flow.

For the most efficient interchange of fluid by the tidal flow, the amount of tubing between the empyema cavity and the rubber bag is cut to the minimum.

Numerous types of rubber bags have been tried, such as the Vorhees bag, blood pressure cuff, mouth piece for a gas anesthesia machine, and others. It is desirable, however, to have a bag with the tube entering it about the middle of the longitudinal axis; a football bladder best meets this requirement. There are two distinct advantages in this type of bag:



Fig. 3.—Close view of the apparatus shown in figure 2, and with the short tube strapped in the chest with adhesive; the tube to the football bladder, which had just replaced an old blood pressure cuff, was later shortened. The lower end of the bladder is turned in to diminish its size. The only care which this case demanded was observation for the proper distribution of the time between irrigation and suction, and renewal of the adhesive dressings about once every two weeks.

The first advantage is that all particles of fibrin and coagulated pus will settle to the dependent point away from the opening of the tube, so that when they enter the bag they are trapped. Incidentally, the tube in the chest entering at the dependent part of the empyema cavity tends to remove the thicker material as it settles out. The second advantage comes into play late in the treatment, after the tube in the chest becomes a little loose. At that time any air which may enter the irrigation system rises to the top and is trapped as soon as it is forced into the bag. The

The frequency with which the fluid should be renewed within the bag depends on the individual case. Early in the treatment, or when the cavity is large, it is renewed every hour in order to keep the pus relatively thin, while later, when the cavity is small and clean, the bag can be refilled only a few times within the twenty-four hours. This avoids disturbing the patient at night, but at the same time gives him the advantage of continuous irrigation.

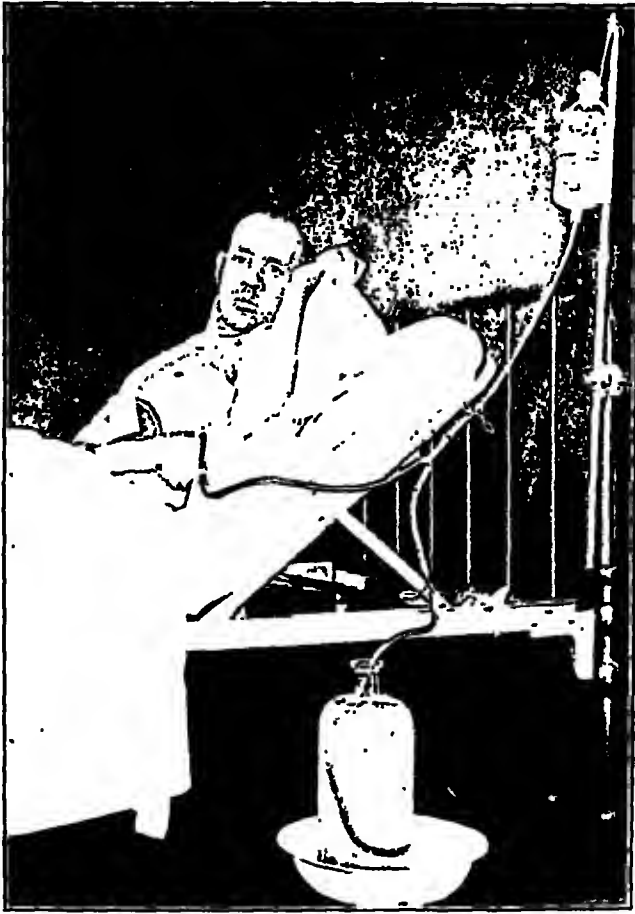


Fig. 2.—Irrigation apparatus in use. This photograph was taken after six weeks of treatment, the patient having a massive hemothorax with infection (figs. 3, 4, and 5). Not once during this time did the tube become plugged; the adhesive holding the tube in place was not changed during the first month, and the apparatus was out of order on only one occasion when the patient, while delirious, left his bed and pulled the irrigation bottle from its stand.

The proportion of time given over to suction and to irrigation depends entirely on the amount and rate of formation of pus. My plan has been to run the irrigation as much of the time as is necessary to keep the cavity clean and the contained fluid thin and relatively clear. The remainder of the time is given over to suction by the siphon. With the bag strapped to the body a little below the level of the empyema

who have gone for from four to seven weeks without having the original tube removed or plugged at any time. One patient (figs. 2 and 3) went for a month without having the adhesive and small dressing about the tube removed, and at no time was there plugging of the tube or any cessation in the tidal flow of the fluid. Consequently, there was at no time any positive pressure of sufficient degree to force fluid out around the tube; also there was no suction of air as the tube fitted

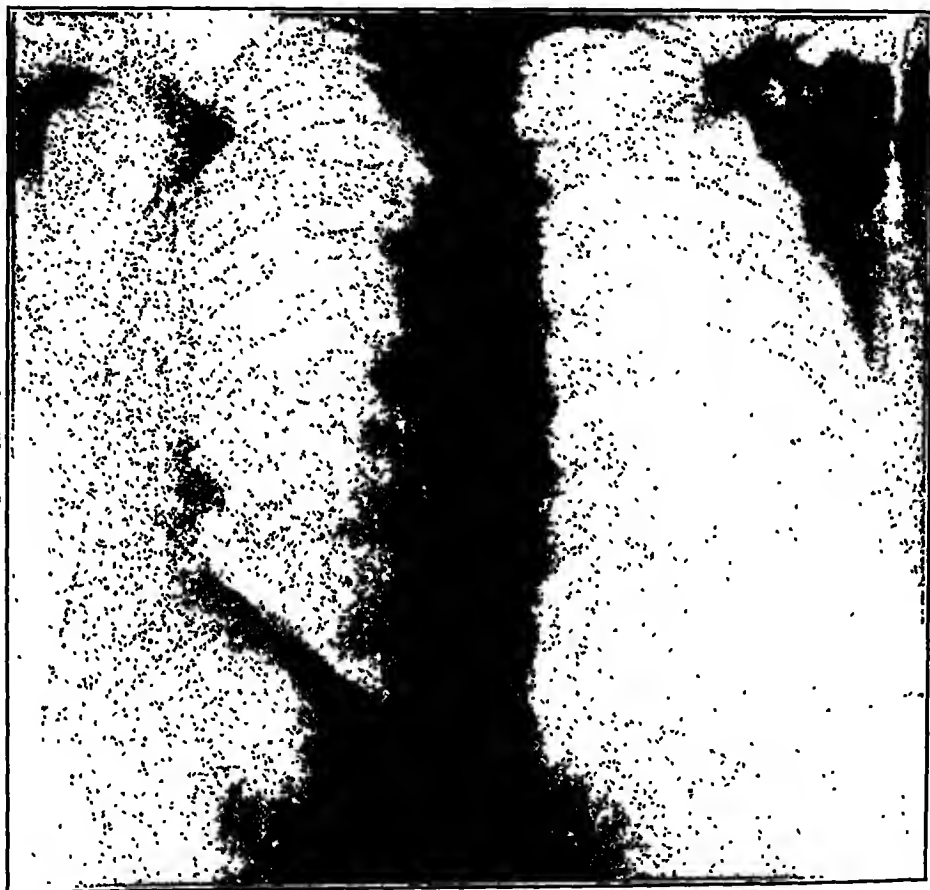


Fig. 5.—Same patient as figure 4, after ten weeks of treatment with continuous irrigation of, or suction on, the empyema cavity. The cavity had completely closed, and the temperature, which had been from 101 to 104 F. before operation, was below 100 F. after the fourth postoperative day. Note the high position of the diaphragm on the left side, its sharp rise from the midline outward until it fuses with the strip of thickened pleura. Below this point it is apparently adherent to the wall of the chest, thus helping to obliterate the empyema cavity after the long collapse of the lung.

The treatment in subsequent cases leads us to believe that the postoperative course here could have been shortened by giving more time to suction, by the earlier institution of forced expiration against an obstacle, with the lungs filled with air, and by inserting the tube through the chest at a lower level.

snugly. At the end of this time, the granulating sinus was free from excessive infection. Another patient went for eight weeks without

thick pus and the air are removed when the fluid within the bag is replenished with fresh solution. Any bubbles of air in the tube to the irrigation bottle are likewise forced into the bag and trapped in its upper part when it is refilled with fresh irrigating fluid.

In the application of this apparatus, the fluid cannot be forced into the chest as long as the rubber bag is not more than from two-thirds to three-fourths full, and frequently it is kept only from one-third to one-fourth full. For children, the lower end of the bag is sometimes



Fig. 4.—An enormous, infected left hemothorax following a stab wound of the chest. Over a period of two months repeated efforts were made to aspirate the fluid, but without result. The collection of fluid increased in size and there was a progressive rise of temperature until the clot became sufficiently fluid to aspirate. The fluid promptly reformed, the cultures were positive for *Streptococcus viridans*, and a trocar thoracotomy was performed.

turned in, as in figures 2 and 3, the size thus being decreased. This absence of positive pressure prevents the forcing of infected material out around the tube, particularly when the cavity has closed down until it holds only a few cubic centimeters, less than the amount of the tidal flow in the beginning of the treatment, and when one's tendency is to run in more solution than the cavity will hold.

The continuous movement of the fluid prevents any coagulation of fibrin and blocking of the tube. This has been proved by several patients



tidal irrigation of the empyema cavity where the apparatus is in use. The blowing is also most efficient when this apparatus is applied, for there is absolutely free egress of fluid when pressure is made on the cavity by the forced expiration. Suction can be applied as desired to hold the lung in the position of expansion or to aid in the expansion obtained by forced expiration with the lungs full of air.



Fig. 7.—Same chest as shown in figure 6, after twenty-four days of treatment by continuous tidal irrigation and suction. The patient was ill, and following operation there was a sharp rise of temperature to 104 F., with a drop to 100 F. the following morning. There was immediate and constant improvement, the patient's temperature remaining around 99 F. to 100 F., with a few elevations explainable by severe abscesses over the back. At the time this picture was taken the cavity holds less than 8 cc., and a rapid healing is anticipated.

With this opening freely patent at all times, and with the continuous irrigation, the drainage must be as good as, if not better than, with a rib resection and a larger opening.



cavity not surrounded by dense scar tissue. With the tube to the drainage bottle open, there was still considerable pressure within the rubber bag, and this could not be relieved until the drainage tube was emptied of fluid and its lower end raised above the level of the fluid in the drainage bottle.

To overcome this complication, the apparatus illustrated in figure 10 was devised. This consists of a flask partially filled with irrigating fluid, connected by an opening at its dependent part to a short tube entering the empyema cavity. An irrigation bottle is connected to an opening at the top of the flask, while through a cork is passed a tube opening to



Fig. 9.—Same chest as in figure 8 after forty-eight hours of treatment with continuous tidal irrigation. The pus was thick, but the tidal flow was perfectly satisfactory for the first fifteen hours.

Apparently at that time the lung had expanded sufficiently to permit of the two pleural surfaces rubbing together with the respiratory movements, and the shaggy exudate over the surface was dislodged. As soon as this was removed from the empyema cavity by manipulating the tube and by frequent irrigations, there was no further embarrassment to the free flow of the tidal irrigation, and there have been no other large masses of fibrin.

In the early morning at the time of the freeing of the large amount of fibrin and exudate, the patient's temperature was 104 F. However, forty-eight hours after the thoracotomy was performed, the temperature remained below 100 F. for the entire day.

As far as could be determined at that time, there was only a small amount of fluid within the empyema cavity.

Not the least of the advantages is the interest which the patient manifests in the irrigation. This applies equally to the child, who is proud of the apparatus and treats it like a toy, watching the motion of the fluid and the particles of pus darting back and forth, and to the adult, who on seeing flakes of fibrin in the tube moving with the tidal flow, will deliberately, with a long and forced expiration, force them into the bag, where they settle down to the bottom and are eventually siphoned off to the drainage bottle.



Fig. 8.—Chest of a boy, aged 5, with a pneumococcus, type IV, empyema. The history suggested the onset with pneumonia for a week, followed by the empyema, which had been present for five weeks. Over this period there had been pain in the chest, high fever, sweats, and a progressively downhill course.

#### ACUTE EMPYEMA COMPLICATED BY BRONCHIAL FISTULA

In cases of acute empyema with a bronchial fistula in which the patient did not cough up the pus from the cavity, irrigation was tried. If, as frequently happened, this did not produce irritation and coughing, the irrigation apparatus shown in figures 1, 2 and 3 was used. This proved to be unsatisfactory, however, since the continual leakage of air into the empyema cavity soon filled the rubber bag with air until it was under marked pressure. There must of necessity have been some associated compression of the lung where the empyema was acute and the

harm comes from the entrance of air into the chest, since it is continually coming in through the bronchial fistula, while if the siphoning action is destroyed by air entering the tube, it is readily reestablished by closing clamp *c*, clamping off the tube to the empyema cavity, and opening clamps *a* and *b*. Suction can be applied as desired by closing clamp *c* with the flask relatively full, and opening the siphon on a closed cavity by removal of clamp *b*. By this means it can be determined when the fistula is closed, suction can be used as desired, and after it is proved



Fig. 11.—Chest of a girl, aged 5, with an acute pyopneumothorax of unknown duration, just before a trocar thoracotomy was performed. A bronchial fistula was present, and the cavity was treated by continuous tidal irrigation, using the apparatus shown in figure 10. The temperature dropped to normal and remained below 100 F. for the postoperative course.

that there is no further leak, the case can be treated like a simple empyema.

This apparatus is to a certain extent cumbersome, and demands rather careful adjustment; the flask cannot be completely emptied, and the opening to the chest is near the bottom of the flask where the thicker pus collects. However, it has proved satisfactory in the cases in which it was used. It seems likely that it will be desirable to replace it by a rubber bag, which provides for the ready escape of the air which enters from the bronchial fistula.



There is only late and negligible leakage around the tube in the thoracotomy wound, so that dissecting infections do not occur, and dressings are practically eliminated.

Suction can be applied as desired, even as long as from six to eight weeks after operation, when expansion of the lung is slow after long compression. Even then there is little if any leakage of air around the tube in the thoracotomy wound.

The apparatus used in the presence of a bronchial fistula permits the immediate escape of air from the drainage system without the possibility of the air reentering the chest or disturbing the siphoning action.

By this method of treatment, the closing of the empyema cavity is more rapid than by the early institution of rib resection and open drainage.

With the use of the flask there is the least limitation to the movements of the patient and the minimal traction on the tube entering the chest; and every possibility of spilling the irrigation solution in bed is avoided by suspending the flask from an overhead frame so that it just clears the bed and normally hangs immediately adjacent to the thoracotomy opening.

#### SUMMARY

A method is described with illustrations of the apparatus used in treating patients who have acute empyema, with or without the compli-



Fig. 12.—Same chest as figure 11, taken on the thirteenth postoperative day. At this time the tidal irrigation system ceased to work, and on attempting to open the tube it was found that there was no cavity, but only a sinus the size of the rubber tube. The patient is apparently well, free from pain, and playing, with a normal temperature and practically no drainage from the sinus.

cation of a bronchial fistula, by continuous tidal irrigation carried on by the normal respiratory movements.

The trocar thoracotomy subjects the patient to the minimal operative procedure.

As the irrigation tube practically never becomes plugged, there is no obstruction to free drainage. In addition, the cavity is being continually washed out by relatively clean solution, so that there is more efficient cleansing and drainage than with the rib resection and open thoracotomy.

There is not the large raw surface to become infected by the continual soiling at the time of and following operation.



*Operation.*—June 12, 1922: The operation was performed by me with Drs. Woodruff and Lutterloh assisting. Ether anesthesia was given by Dr. Allgeyer. A preanesthetic hypodermic injection of one-fourth grain (0.016 Gm.) of morphine and one one hundred and fiftieth grain (0.0019 Gm.) of atropine was given. The anesthetic was started at 10:47 a. m., and discontinued at 12:06. The operation was started at 11 and was discontinued at 12:12, the procedure consisting of excision of the neuroma and transplantation of the median nerve into the ulnar nerve in the right arm.

An incision about  $3\frac{1}{2}$  inches (8.87 cm.) long was made on the inner side of the biceps muscle corresponding to the course of the brachial artery. As soon as the soft tissue was dissected away and the muscles retracted, the large mass with the blood vessels came into view. The median nerve was isolated above the level of the tumor and a pair of forceps insinuated between the brachial artery and the median nerve to act as a support. After this the dissection of the tumor, which was continuous with the median nerve, was carried on, and the mass entirely separated from the brachial artery. It was shown to be a spindle-shaped mass about  $2\frac{1}{2}$  inches (6.27 cm.) in its long axis and  $\frac{3}{4}$  inch (1.9 cm.) transversely. In one place on the outer aspect of the mass, it had broken through as

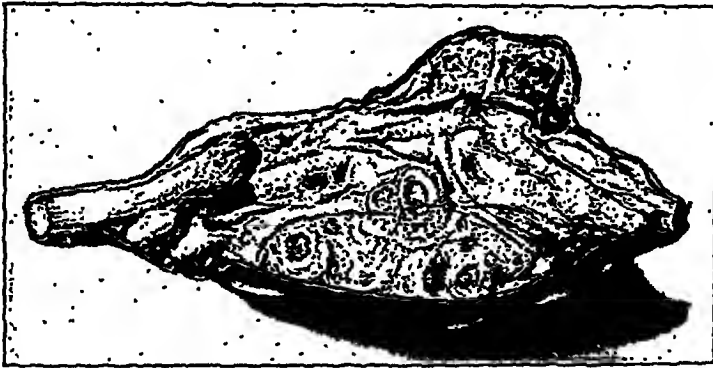


Fig. 1 (case 1).—Gross specimen of tumor of median nerve.

though there had been a slight hemorrhage. The lower limit of the tumor was just above the bicipital fascia (fig. 1).

Procaine hydrochloride was injected into the median nerve above the level of the neuroma, and a section was made of the nerve above. Then the nerve was sectioned below. This left a distinct gap of about  $3\frac{1}{2}$  inches. It was impossible to consider elongation of the nerve to close the defect, and therefore the question of where to graft the distal end was considered. It was decided to utilize the ulnar nerve. This was exposed behind the internal condyle and isolated and mobilized. A tunnel was made under the pronator teres with a pair of forceps. The distal end of the median nerve was brought under the tunnel and grafted into the lateral aspect of the ulna with fine silk. The proximal end of the nerve, which was cut instead of being left unattached, was sutured to the internal cutaneous nerve, which was exposed in the wound. The wound was sutured in tiers with fine catgut to approximate the muscle and subcutaneous tissue. Michel's clips were used for the skin. Cross-section of the tumor showed that it contained a good deal of connective tissue and some degenerating areas which looked like colloidal material. A diagnosis of neuromyxosarcoma was made.

Laboratory examination showed a somewhat cylindric-shaped structure measuring 7 cm. in length and 3 cm. at its broadest diameter. It tapered at each



structure-like material. They were lined with cells that were tall and columnar in their general appearance, which were closely packed together, and on close study showed practically no separation of the individual cells; the appearance was that of a multinucleated syncytial mass resting on an underlying structure resembling a basement membrane. The entire glandular structure was divided into areas of various sizes by a cellular supportive material showing nuclei occupying a relatively large proportion of the cell; there was a minimum amount of intercellular substance. Most of the supportive structure was suggestive of nerve tissue, but I was unable to find positive evidence of a former nerve trunk anywhere except on the periphery. Mitotic figures were noted both in the epithelial and supportive cells. The blood supply of the part was not prominent, the vessels being present in stroma. A few areas of necrosis and degeneration were noted, but these were confined largely to the glandlike spaces. In some places, the stroma was myxomatous, and in others, it was made up of a denser tissue.



Fig. 3 (case 1).—High power magnification of first recurrence showing glandular elements.

A tentative diagnosis of carcinoma of the gland cell type was made, with the explanation that further study was required to determine definitely the primary origin (Lanford).

*Progress Notes.*—Following the operation, the patient had a sensation of pain and touch in the thumb and all fingers. He was able to flex and extend his wrist. Three days after operation, common sensation was noted in the peripheral distribution of the median nerve. The wound healed by primary intention. When the patient left the hospital ten days after the operation, common sensation was present as already noted.

During October, 1922, the patient returned, because a painful lump had developed in the upper portion of the wound caused by the previous operation. This was believed to be neuroma of the stump of the median nerve, and operation was advised.



*Progress Notes.*—On June 23, 1923, the patient returned because of the development of a mass on the inner aspect of the elbow. Examination at this time revealed the following: The patient was well developed and did not show any evidence of emaciation. With the exception of the tumor mass at the elbow, nothing in his condition indicated general discomfort. The scar of the previous operation on the right arm was healthy. The elbow was flexed at a right angle. There was little mobility of the joint, and the forearm was midway between pronation and supination. Some atrophy of the muscles of the hand was present, but sensation of pain, touch and temperature in the forearm was undisturbed. However, there was some diminution of sensation in the index finger.

Dr. Holbrook, a neurologist, examined the patient and reported: "Sensation of pin and cotton is good over the palmar surface of the right hand, except in

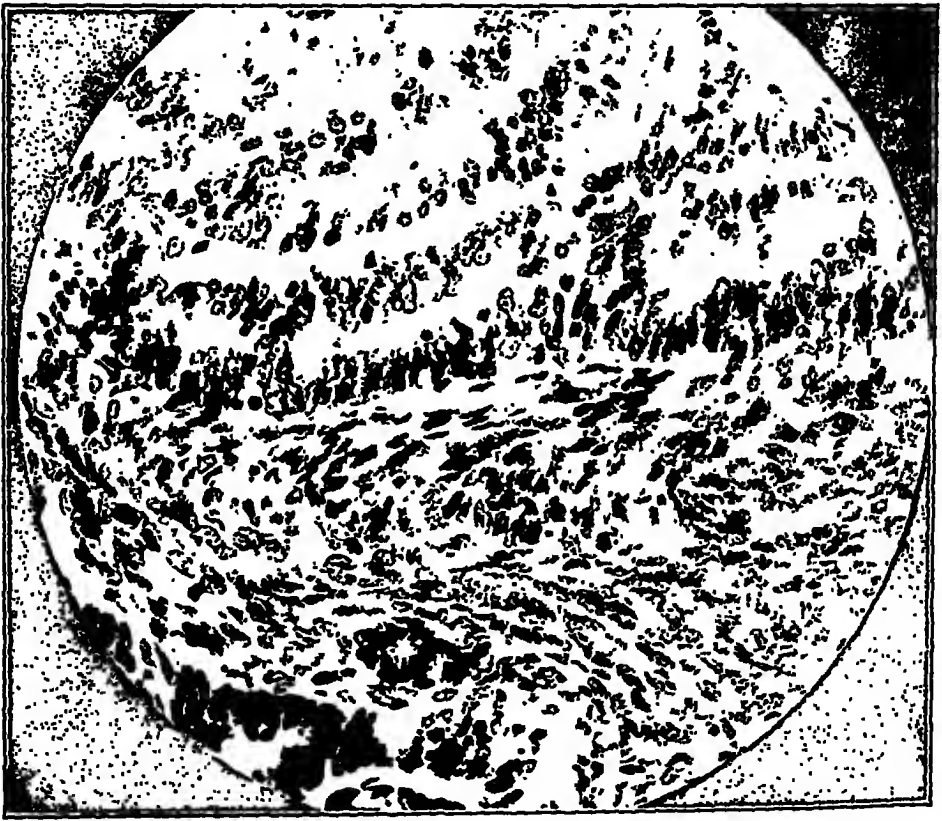


Fig. 5 (case 1).—High power magnification of first recurrence.

the index finger, in which sensation is dulled about the middle and beyond this point is absent. Thermal sensation is inaccurate over most of the hand, especially toward the index finger. Temperature differences are appreciated toward the center and inner side of the hand."

*Third Operation.*—On Jan. 25, 1923, I performed an operation with Drs. Macheca and Liles assisting. Dr. Allgeyer gave the ether anesthesia.

The amputation was made at the junction of the middle and upper thirds of the right arm. A tourniquet was applied, a circular skin flap dissected up, and the muscle cut at the level of skin retraction. The muscles were retracted and the humerus sawed through. The large nerves were then brought down into the field, and an inverted V-shaped excision of the end approximated the sheaths



median nerve at its anastomosis with the ulna. The belly of the flexor sublimis digitorum was ballooned out by the growth and gave the appearance of a funnel. In order to disturb the appearance as little as possible, Dr. Lanford took a small block of the tumor out of the ballooned portion of the palmaris longus belly. This was then sutured in order to retain the contour of the original growth.

Laboratory examination showed a specimen made up of the forearm and hand and about 6 inches (15.24 cm.) of the arm, which presented a tumor involving the structures at the bend of the elbow. In gross, the hand showed considerable atrophy changes, but otherwise was normal. A marked swelling was noted mostly at the bend of the elbow on the anterior surface, extending backward and laterally to involve most of the structures. The overlying skin was intact and loose over the growth, and there was a long, well healed scar from a former

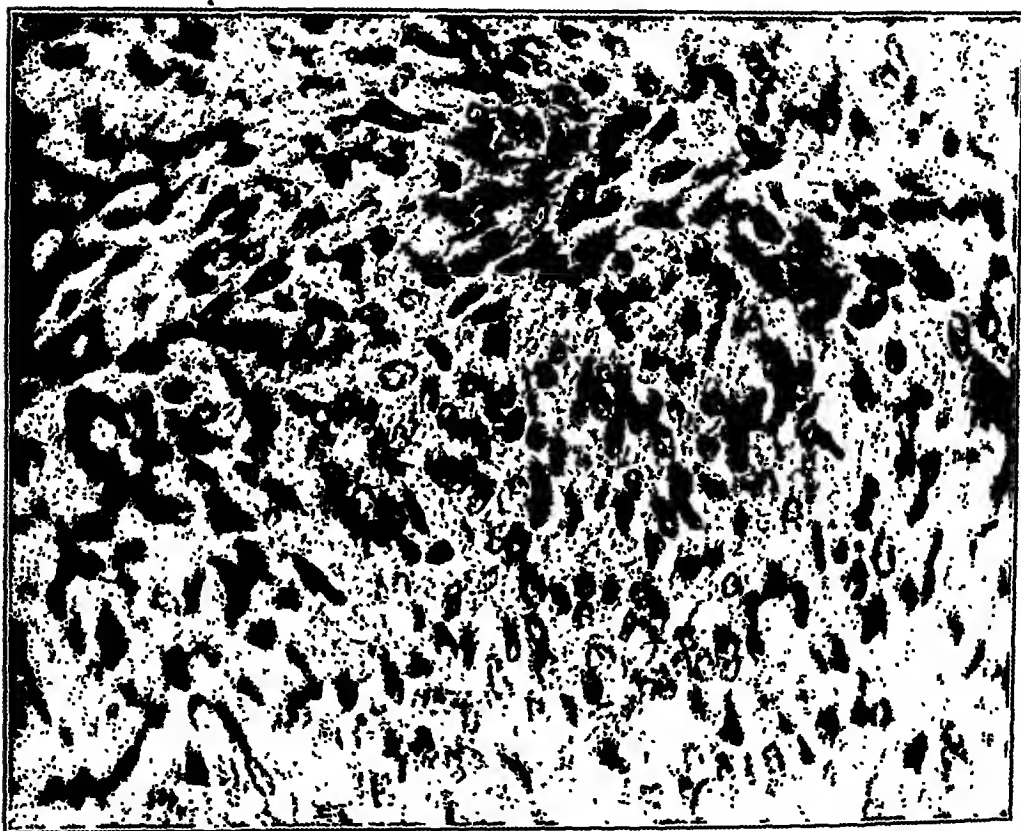


Fig. 7 (case 1).—High power magnification of second recurrence.

operative procedure. When the skin was dissected back, a new growth was found that had involved the muscles of the part, particularly all those inserted into the internal condyle of the humerus, and to a lesser degree those of the external condyle. The muscles were pushed upward and were thinned out, this being particularly noticeable in the superficial layer, while the deeper layer was more infiltrated and replaced by the main growth. The main mass was 11 cm. in length and 8 cm. at its thickest portion; it was roughly cylindric or funnel-shaped, the upper portion being at the bend of the elbow, and the pointed end extending onto the forearm. It was firm, and here and there presented nodulations which were smooth and were firmly adherent to the overlying muscle. On sectioning, it offered considerable resistance to the knife and presented a cut surface that was

with plain catgut, making a fish-tail appearance after the suggestion of Corner. The nerves were injected with 95 per cent alcohol following the suggestion of Carl Hoover and Lewis. The muscles were quilted over with plain catgut after ligation of the large vessels. Chromic catgut no. 2 was used for ligation. There was little bleeding. Interrupted plain catgut sutures were introduced into the sheath to diminish the amount of dead space. The skin was closed with silkworm and plain catgut interrupted sutures. The specimen was sent to the laboratory for preservation. Amputation was done because the removal of sufficient tissue to remove the entire mass would leave a useless arm.

A gross specimen was taken from an amputation of the lower third of the arm and forearm. The dissection was done by Dr. Lanford, and the line of the previous incision along the course of the ulnar nerve was incised. The skin

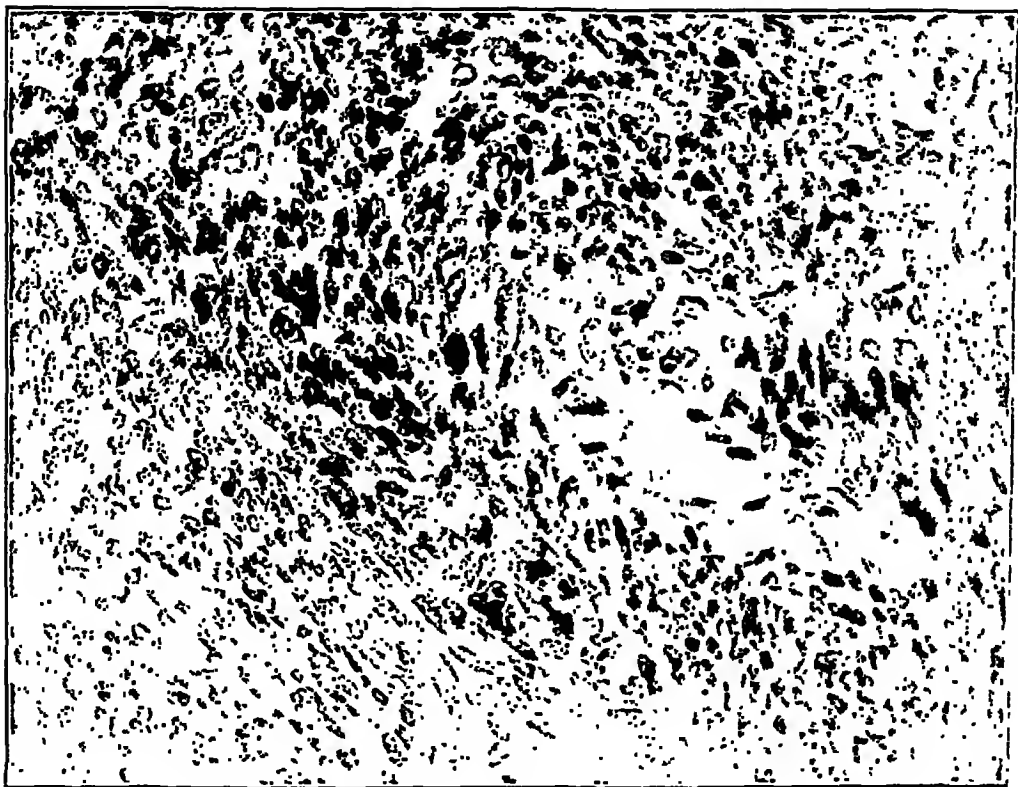


Fig. 6 (case 1).—High power magnification of first recurrence. The glandular elements are being crowded out by the embryonal character of the stroma cells.

and fat were retracted. The ulnar nerve, prior to its entry into the pronator teres, was exposed and the nerve followed down to a point where it was lost in the tumor mass just above the internal condyle. The skin flap was then dissected away from the muscle, exposing the biceps and the tumor mass, which was covered by the flexor muscle originating from the internal condyle. The brachial artery was then retracted medial to the ulnar side, exposing the median nerve below. We then followed the median nerve to its point of implantation into the ulna by cutting through the pronator teres and palmaris longus muscle below. We could see the suture line as evidenced by the black silk which had been used a year ago. There was apparently no thickening of the exposed portion of



When last heard from, four years after operation, he weighed 200 pounds (90.7 Kg.) and was in excellent health.

*Summary.*—1. A patient with von Recklinghausen's disease presented a tumor of a peripheral nerve.

2. The tumor resembled a carcinoma. It was made up of glandlike spaces lined by columnar cells with little separation of the individual cells, which gave the appearance of a syncytial mass. Mitoses were noted.

3. After excision of the tumor, recurrence occurred in the stump.

4. Histologically, this resembled the primary tumor.

5. A second recurrence necessitated amputation.



Fig. 9.—Low power magnification of first recurrence tumor of the radial nerve.

6. This tumor contained spindle-shaped cells. There were small cavities which were lined with a single layer of cells resembling epithelium.

7. The patient remained well for at least four and one-half years. Since that time, we have been unable to trace him.

8. The tumor was epithelial.

9. It caused expansion of the nerve and disturbance of the peripheral distribution of the nerve.

10. There were no distant metastases.

Certain questions naturally arise: 1. What is the origin of a tumor of the nerve which is epithelial? 2. Is it part of a systemic disease? 3. What is its relation to von Recklinghausen's disease? 4. Did it come

grayish white and apparently made up largely of supportive tissue. The bands of tissue running in all directions gave somewhat the appearance of a leiomyoma of the uterus. The blood vessels were not prominent, and only here and there were areas noted which appeared to be well supplied with blood. An occasional area on the cut surface was noted which showed degeneration suggestive of a myxomatous or loose, meshlike type of structure containing a clear pinkish stained serum, but no definite lobulation or cystic cavity could be found.

Microscopic study showed the mass to be almost uniformly made up of spindle-shaped cells running in bundles in all directions. Some of these strands were considerably older than others and tended to separate the more rapidly growing ones into distinct areas. Here and there little microscopic cavities could be noted



Fig. 8 (case 1).—Patient several months after amputation.

that were lined with a single layer of cells resembling epithelium. The blood vessels were not prominent in the main portion, although here and there a few capillaries were noted. Some of the older portions of the growth showed considerable deposition of collagen-like material, and still others were somewhat myxomatous. Many of the cells were rapidly growing and showed mitotic figures. The histology was that of a neurogenic sarcoma, with absence of the glandlike spaces noted in the primary growth.

*Progress Notes.*—On June 29, the wound was dressed. Swelling was not great. Primary union occurred and the patient was permitted to go home, but was kept under observation for more than a year. His general condition continued good with no evidence of recurrence or development of the tumor in any other part.

After twenty years of experimental observations (1904-1924), Harrison<sup>3</sup> stated:

One who follows historically the subject of the histogenesis of the nervous system cannot but be impressed by the deviousness of the path of progress.

With the foundation of the neuron theory by His (1886) and Forel (1887) the study of the nervous system entered upon its modern phase.

The investigation of His (1886, 1887, 1888, 1890) followed by the work of Ramon y Cajal (1890, 1892, 1894), who first applied the Golgi method to the study of the embryonic nervous system, and that of v. Lenhossek (1892, 1895), gave a firm footing to the concept of the neuron by showing clearly, as it then seemed, that each fiber arises as the outgrowths of the single ganglion cell.

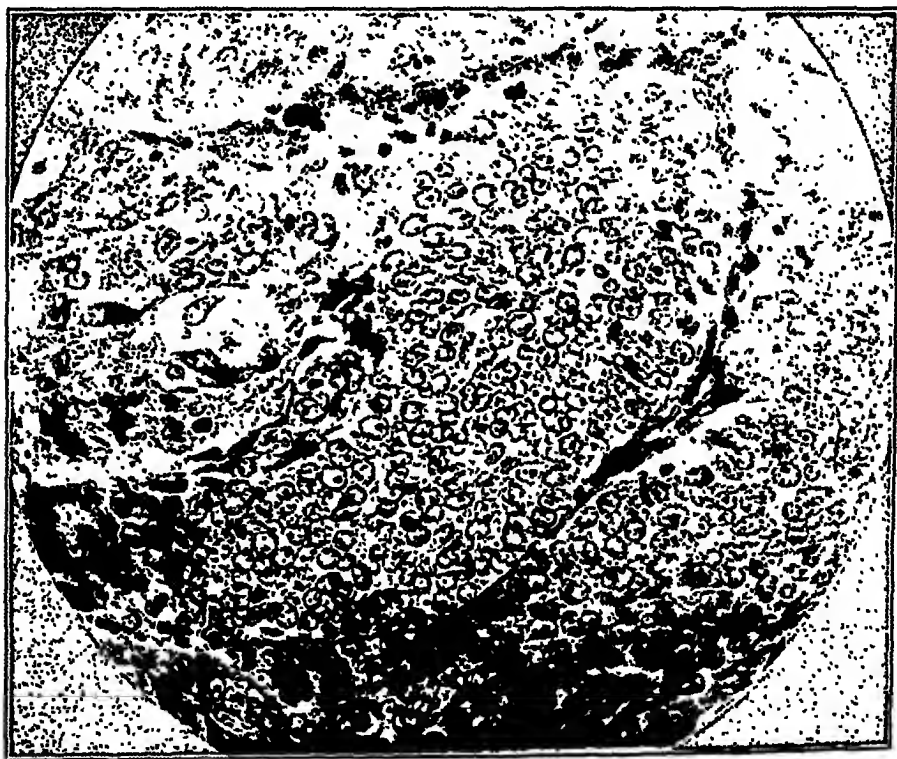


Fig. 10.—High power magnification of first recurrence.

Experiments, with hanging-drop cultures of embryonic nervous tissue in clotted lymph, rendered possible the direct observation of the growing nerve fiber, showing the latter to be not a chain of cells, but a strand of hyaline protoplasm with an active amoeboid end, through the motion of which the fiber is spun. In other words, it was actually seen that nerve fibers grow as the process of a single neuroblast.

To sum up the impression gained from the study of the relevant literature accumulated since 1900, we find that the neuron concept, so far as it applied to the development and regeneration of the nervous system, remains unshaken under the attacks it has received, and that it now stands more firmly established than ever.

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3. Harrison, Ross G.: Neuroblast Versus Sheath Cell in the Development of Peripheral Nerves, *J. Comp. Neurol.* 37:123 (June) 1924.

from a misplaced cell rest or can it be explained by referring to the histogenesis of some element of nerve tissue?

Tumors of the peripheral nerve must originate (1) from some constituent of the nerve; (2) from misplaced cells; (3) be part of a systemic disease, or (4) be metastatic growths.

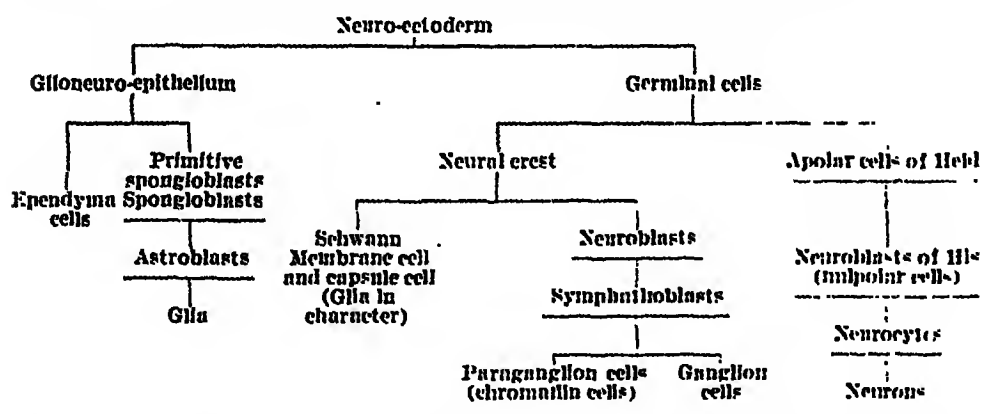
To develop the subject, it will be necessary to introduce a brief review of the embryology of the nervous system and the facts as well as the theories available in the literature.

Some of the following data are essentially academic, but necessary to present the subject clearly.

*Embryology.*—According to Hardesty: <sup>1</sup>

The essential elements of the nervous system, the nerve cell-bodies and the essential portion of all nerve fibers, central craniospinal and sympathetic, develop from one of the embryonic germ layers, the ectoderm, and all arise from a given

*Histogenesis of Nervous System (Glober and Strauss)*



region of that layer. Further a small portion of the supporting tissue of the nervous system the neuroglia, is of the same origin.

*Peripheral Nerves.*—According to Stookey: <sup>2</sup>

A typical peripheral nerve is made up of neuraxes from nerve cells either within the brain stem and spinal cord, or from cells of the spinal, cranial and sympathetic ganglia.

Two main theories have been offered concerning the origin of the neuraxes, one the outgrowth theory of His (1890) and the other the cell chain theory of Bethe (1903) and others. A still older theory is that of Henson, according to which there always are protoplasmic intercellular bridges in the developing embryo and out of certain of these bridges the nerve fiber is differentiated. Held (1909) has supported a modification of this theory, according to him the nerve fibers differentiate from the nerve cell bodies along these protoplasmic bridges.

1. Hardesty, Irving: The Development of the Nervous System, in Morris' Human Anatomy, Philadelphia, P. Blakiston's Son & Company, p. 754

2. Stookey, Byron: Surgical and Mechanical Treatment of the Peripheral Nerves, Philadelphia, W. B. Saunders Company, 1922.

Both medullated and nonmedullated fibers are assembled in nerve bundles called funiculi, and the funiculi in turn are joined together into a larger group by a surrounding sheath of connective tissue called epineurium, thus forming a peripheral nerve. The individual fibers of the funiculi are separated by a small amount of connective tissue called endoneurium and the funiculi are surrounded by a lamillated layer of fibrous tissue which encircles the funiculi, called by Key and Retzius (1873) perineurium.

The origin of the cells of the sheath of Schwann has been a cause of great controversies.

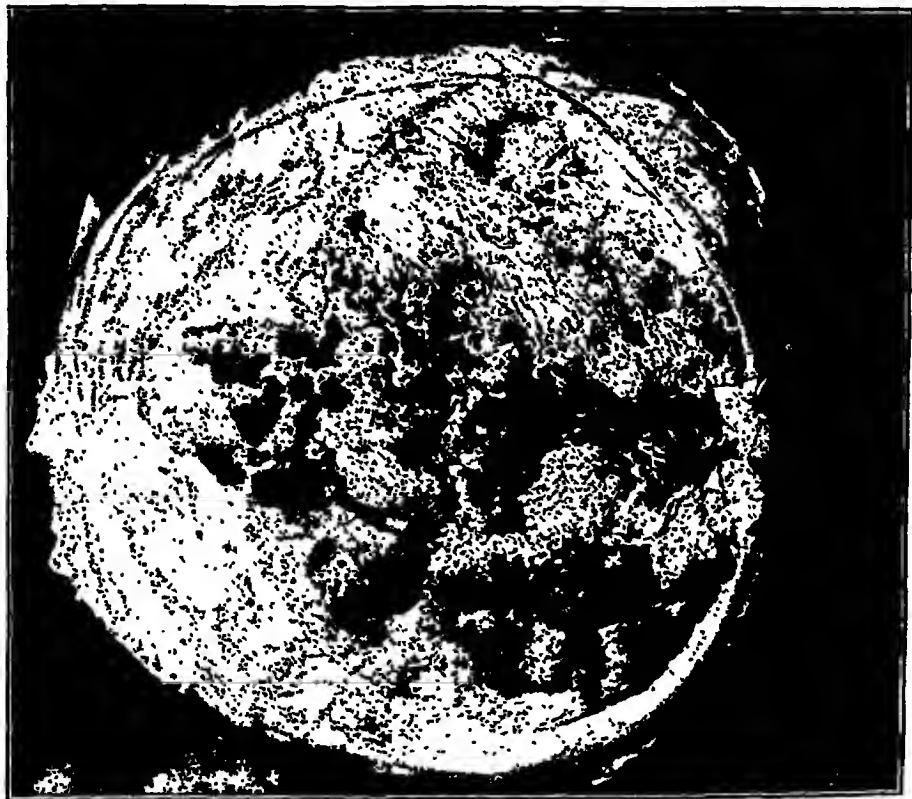


Fig. 12.—Upper surface of dura.

Two main views have been held concerning the origin of these cells it being formerly thought that the sheath was of mesodermal origin. The more recent view on the other hand has been that the sheath cells were closely related to neuroglia and were of ectodermal.

The latter theory has been proved by Harrison's ganglion excision experiments.

By excising the gauglionic crest of young amphibian embryos peripheral motor nerves, in the form of naked axis cylinders, developed in place of nerves which normally had numerous spindle shaped sheath cells about them.

The experiments leading to this conclusion have recently been repeated by Muller and Ingver (1921) with like results.

The problem before us is, simply how the axon is constituted in development—whether it takes origin from a cell chain, or is the process of a single ganglion cell.

The method of procedure was to eliminate by appropriate operation first the source of the sheath cells, and, second, that of the motor ganglion cells.

The development of the axon is a function of the neuroblast.

The removal of any body of neuroblasts invariably results in the elimination of the peripheral nerves normally connected with them.

I may therefore proceed with the study of the development of the peripheral nerves, accepting as a proved fact that the neuraxis or axon is a product of the neuroblast, and continue to construct my concep-



Fig. 11.—Dissection of amputated limb.

tion of the development of the remaining portions of the peripheral nerve.

According to Stookey:

The neuraxis extended without interruption from the cell of origin to its ultimate termination. It consists of neurofibrils imbedded in a semifluid neuroplasm and surrounded by a very delicate membrane, the axolemma. The fibers are described as of two types, medullated, and nonmedullated, depending upon the presence or absence of a sheath known as a medullary or myelin sheath. The medullary sheath contains myelin—a chemical substance made up largely of lecithin, and supported by a framework or neurokeratin. Outside of the myelin is a delicate nucleated sheath known as the sheath of Schwann or neurolemma. The nonmedullated fibers of the peripheral nerves arise from the cells of the sympathetic and spinal ganglia.

The outstanding point today is the origin of the "connective tissue which immediately surrounds the nerve elements." Is he referring to the sheath of Schwann? That the type of cell which is its progenitor is ectodermal has apparently been settled by the experimental work of Harrison.

In 1908, Verocay<sup>6</sup> studied a specimen from a case in which he had performed the autopsy. The case presented "multiple tumors in the central nervous system and its meninges as well as in the course of the peripheral nerves." He presented the case hoping that it may help in



Fig. 16.—Tumor involving entire right lung showing occlusion of bronchus.

this way to clear up a rather obscure field in the pathology of the nervous system.

His expectations have been more than realized, because all students of this subject refer to him as the first to express the idea of the association of peripheral and central nerve growths and the ectodermal origin of these peripheral tumors (sheath of Schwann).

He said:

The old dispute over the nature of Schwann's cells has at present been settled by showing that they are of ectodermal origin and that they originate from the same anlage as the specific nerve cells-nerve cells and glia cells.

6. Verocay, Jose: Multiple Tumors as a System Disease of the Nervous System, *Festschr. f. Hans. Chiari*, 1908, pp. 378-415.

Harrison said:

The sheath cells are best interpreted as a sort of peripheral neuroglia—an idea that has found favor with a number of students of the structure and development of the nervous system.

The sheath cells are clearly separated elements, which are closely applied to the axons. While they have but a small amount of cytoplasm, they are in no sense mere nuclei and part of the axon itself.

It is likewise definitely shown that the sheath cells are not mesodermal, but arise for the most part from the ganglion crest in connection with the spinal ganglia. Some arise later directly from the medullary cord by emigration along the ventral roots.



Fig. 13.—Gross photograph of brain with dura reflected showing neoplasm pressing on cerebrum.

The sheath cells are to be regarded as the neuroglia of the peripheral nerves.

The literature makes one feel justified in accepting the ectodermal origin of the cells of the sheath of Schwann.

When one turns to clinical experiences, one finds a state of confusion. If Harrison's work is correct, this confusion should cease to exist.

*Pathology.*—Is it possible for an epithelial recurring type of tumor of a peripheral nerve to arise from the elements of peripheral nerve, and may it be a part of a systemic disease, or must it be of metastatic origin?



Serre's paper must be freely abstracted:

The history of neurofibromatosis dates back to Recklinghausen who, in 1882, undertook the synthesis of the sparse findings in the previous observations of dermatologists, surgeons, and anatomic-pathologists.

The histologic conceptions of neurofibromatosis have varied greatly during the course of the last few years. After Virchow, who distinguished pure neuromas mixed neuromas (true neurofibromas) and false neuromas (fibro-myxomas, fibrosarcomas), Recklinghausen, in 1882, grouped all the cases under the heading of fibromas.

To this purely connective conception in which the tumors were considered as being derived from the perineurium, Bard, in 1885, opposed a theory, sanctioned by Durant in which the neurofibroma was derived from the segmentary cell of the nerve fiber. With the investigations of Held and Nageotte on the histology

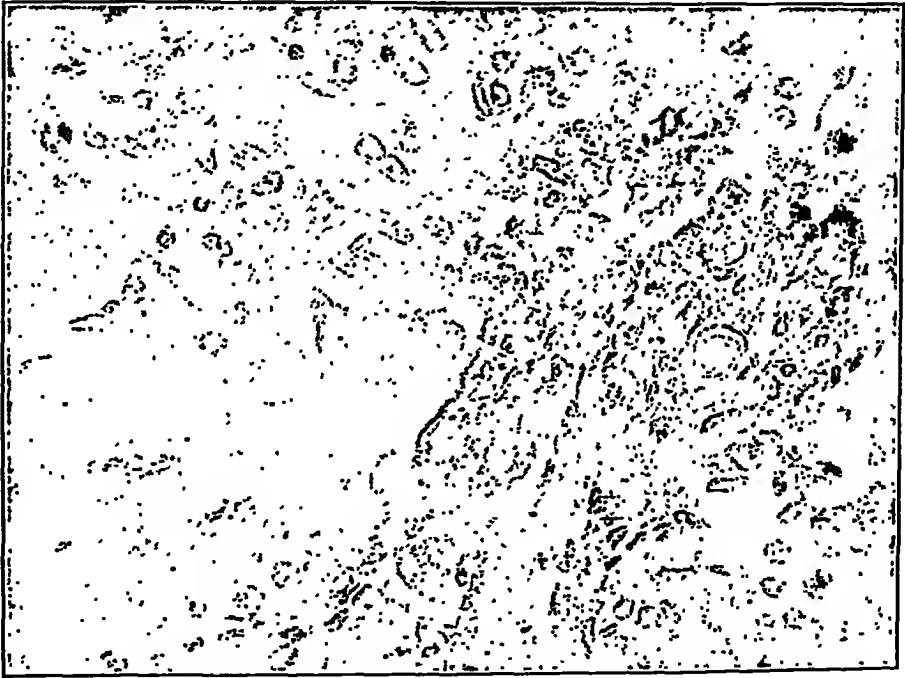


Fig. 18.—High power magnification of tumor of lung.

of the nerves and the works of Verocay, Trapier, Bard, Gall, Gautier, Delore, and especially with the recent studies of Lhermitte and Leroux, there has arisen the new theory of peripheral neurogliomatosis developing at the expense of the sheath of Schwann or the peripheral neuroglia.

Discussing Recklinghausen's disease, he said:

Lhermitte and Leroux state that the constitution of the peripheral tumors in Recklinghausen's disease has the fundamental characteristic of being formed by the combination of two tissues, one a compact tissue resulting from the juxtaposition of fusiform cells, the other more loose and reticulated formed of cells with ramifying protoplasmic expansions which anastomose together.

The compact tissue is formed of fusiform elements parallel to each other forming trabeculae, whorls and bundles. The cell itself has a regular ovoid

He summarized as follows:

The above case was an extensive system disease of the central and peripheral nervous system and its meninges in the form of the multiple tumors of the spinal cord and medulla oblongata (glioma) the nerves (originating from the nerve fiber cells and the connective tissue?) and meninges (endothelioma).

2. This system disease is with great probability to be attributed to a congenital anomaly of development.

3. Tumors of the nerves occur with the picture of "Neurofibromatosis" (fibromatosis-nervorum) or "True multiple neuromas which originate from the so-called nuclei of Schwann's sheath, for which reason they are to be regarded as nerve tumors.



Fig. 17.—Low power magnification of tumor of lung.

4. These nerve tumors may also contain ganglion cells the presence of which seems to be most easily comprehensible if they are regarded as being derived from nerve fiber cells also in the normal development of the sympathetic.

Serre<sup>7</sup> presented two cases with peripheral tumors. He expresses the following positive opinions relative to several questions at issue in cases of tumors of peripheral nerves associated with Recklinghausen's disease: 1. These tumors originate from sheath of Schwann. 2. They are part of a systemic disease. 3. Von Recklinghausen's disease is not mesodermal in origin, but the tumors are "developed at the expense of the sheath of Schwann and hence are of ectodermal origin."

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7. Serre, R.: Contributions to the Study of the Visceral Localization of Recklinghausen's Disease, Thesis, Paris, 1923.

opposed to the appearance of clearly individualized adult connective tissue cells, the cytoplasm of which is never fibrillar.

These tumors in no way resemble fibroids from which they differ by the morphologic appearance of the cells, the vascular alterations and the necrotic areas.

Their cellular irregularities, their well individualized cells, the absence of vessels provided with true walls, their tendency to metastases, in a word, their characteristics of nonencapsulated malignant tumors differentiate them at once from the gliomas which are always encapsulated.

There is no point of equal contact between these peripheral tumors of Recklinghausen's disease and the connective tissue tumors. On the contrary there are four arguments which speak in favor of the neuroglial origin of these tumors.

1. The absence of cellular individualization, the syncytial appearance.



Fig. 20.—Low power magnification of tumor of heart muscle.

2. The collection of the fusiform cells into bands or whorls, resembling the appearance of gliomas forming after amputations.

3. The fibrillation of the protoplasm of the fusiform cells and the equally fibrillary structures of the stellate cells, similar to those seen in the gliomas of the brain (Lhermitte and Leroux).

4. The structure of the vessels, the walls thickened by the fibro-hyaline substance, the vascular obliterations.

We can conclude with Lhermitte and Leroux as to their ectodermic neuroglial, syncytial origin and can consider them as peripheral gliomas developing at the expense of the sheath of Schwann.

Conclusions: In Recklinghausen's disease the tumors are not of the connective tissue type of mesodermic origin. The tumors are all of the neuroglial type and are gliomas developing at the expense of the sheath of Schwann and hence are of ectodermic origin.

elongated nucleus surrounded by ill-defined protoplasm, separating the neighboring cells without cellular individualization, that is to say, the syncytial type. Finally a very important characteristic should be noted—the protoplasm is finely fibrillar.

The constitution of the reticulated tissue is very different from that of the compact tissue. Here the cellular elements are stellate cells with protoplasmic expansions more or less loose and anastomosing with the prolongations of the neighboring elements. The elements like the preceding, present a fibrillary protoplasm.

This general description seems to hold true for all the cutaneous and visceral peripheral nerve tumors of Recklinghausen's disease.

*Nature of the Neoplastic Tissue.*—Let us see now why these tumors may be mistaken for fibrous tumors of connective tissue origin and how they may be distinguished. There are three points to be considered: (1) the presence of



Fig. 19.—Tumor of heart and kidney.

collagen; (2) the morphologic appearance of the cells; (3) the disposition of the vessels.

Is collagen specific of connective tissue cells or vessels?

Up to the last few years it has been considered that the collagen framework of the connective tissue is an integral part of the connective tissue cell.

Lhermitte and Leroux have recently shown, in the case of an intra-ventricular echinococic cyst, that there was precipitation of collagen in the middle of an adult neuroglia tissue.

In Recklinghausen's disease the presence of connective tissue cells cannot be concluded from the presence of collagen.

The morphological appearance of the cells is of capital importance. The cells of these tumors are formed of a protoplasm with indistinct outlines which is prolonged into a very fine fibrillary arborization anastomosing with the arborization of neighboring cells. Sometimes, even, the cytoplasm assumes a more clearly syncytial appearance and many clear nuclei may be found. Finally, under high magnification, the protoplasm is seen to be clearly fibrillar, this being

neoplasm, but our neoplasm did not show the characteristics of a neurogenic sarcoma until two previous growths had been removed.

The arrangement is very suggestive of epithelial origin, especially as the most actively growing cells are in glandular form.

The histology suggests very closely the histology of certain ependymal neoplasms. It is therefore necessary to resort to the theory that this neoplasm sprang from a cell which was carried down from the central nervous system in the development of the median nerve, it having its primary origin in the neuro-epiderm of the developing embryo.

Percival Bailey<sup>9</sup> has described the typical ependynoma as follows:

The tumor is composed of a mosaic of polygonal cells with well defined cell borders and heavy, coarsely granular cytoplasm. The cells are crowded against

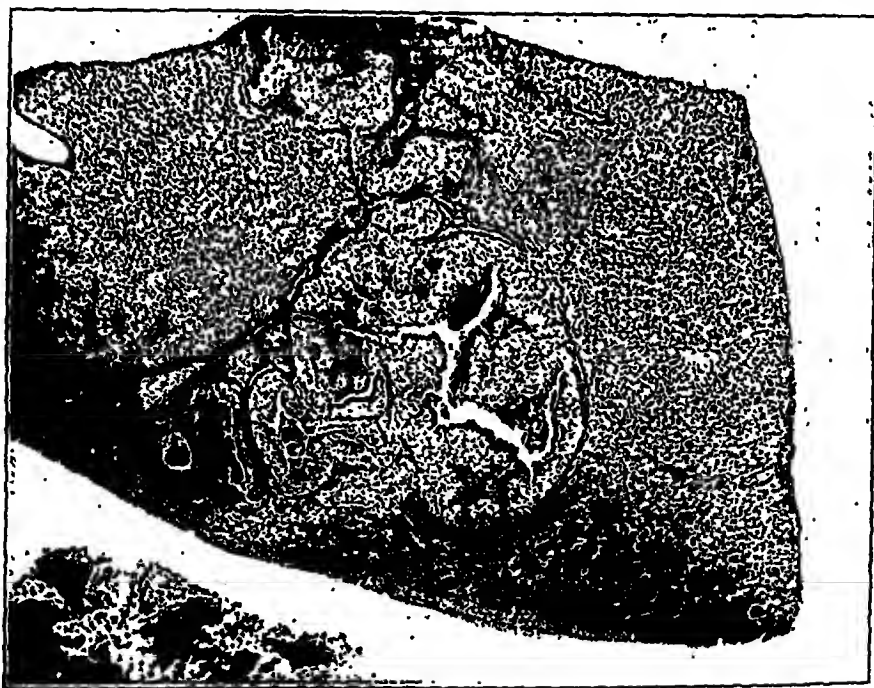


Fig. 22.—Low power magnification of tumor of kidney.

each other and have a single, large, vesicular nucleus. Among them may be seen a few coarse fibrils which stain poorly with methods for the demonstration of neuroglia fibrils. In certain areas the fibrils may be seen to be the continuation of one extremity of the cells. In these areas the cells are apt to have a tendency to arrange themselves radially around blood vessels or around channels whose walls contain a little poorly developed, often hyalinized connective tissue. No other connective tissue is present. In practically all the cells (probably all of the entire cells were included in the section) is to be seen a clear area containing sometimes one, usually two or three, rarely as many as a dozen small, clean-cut markings which stain heavily or by methods for demonstrating neuroglia fibrils, and may be spherical or short bacillus-like rods. These markings we have interpreted as blepharoplasten, or typical of ependymal cells.

9. Bailey, Percival: A Study of Tumors Arising from Ependymal Cells, *Arch. Neurol. & Psychiat.* 11:1 (Jan.) 1924.

Stout<sup>8</sup> reported a case which presented certain points in common with my case. In discussing the case, Stout wrote:

Turning now to tumors arising in the peripheral nerves one is impressed with the fact that the literature is very scanty, but the majority of authors consulted seem to agree that whether single or multiple, malignant or benign, they are of mesodermal origin, coming from the epineural or perineural tissue. In 1906, on the other hand, Verocay described a case with multiple tumors of the nervous system which showed in many of the nodules in the peripheral nerves what he believed to be a marked growth of cells of the sheath of Schwann. He is thus the first author to suggest that the neurilemma cells may be the source of tumors of the peripheral nerves. This view is looked upon with favor by Borst writing in Aschoff's Text Book.

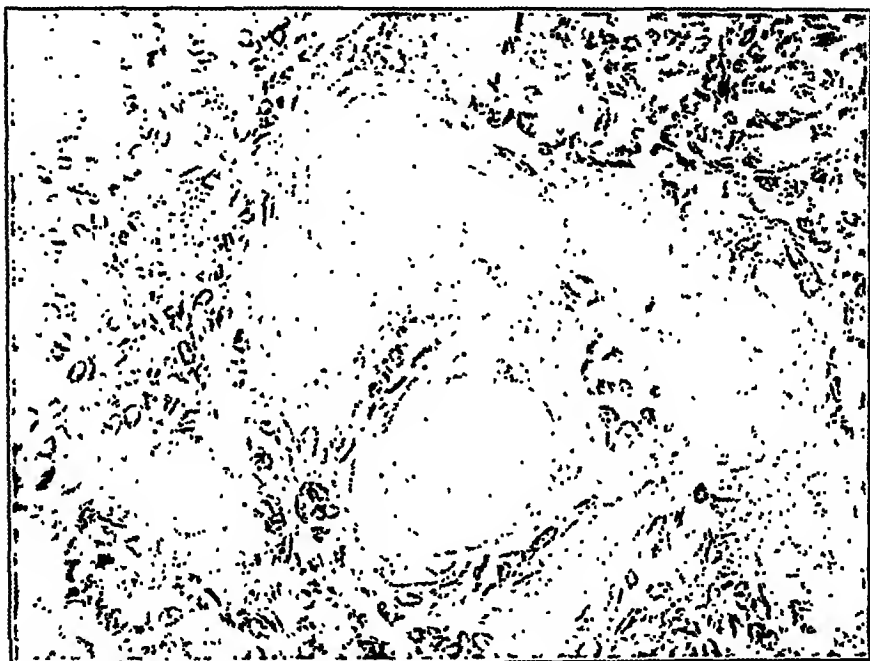


Fig. 21.—High power magnification of tumor of heart muscle.

In conclusion, it may be said that the tumor under consideration is a malignant neoplasm. Since the neurilemma of the peripheral cells is probably homologous to the neuroglia of the central nervous system it is suggested that this tumor may be a neoplasm arising from neurilemma cells or lemmocytes.

Lanford, in a previous report of this case, made the following observations:

Adami quotes Verocay to prove that the cells of the sheath of Schwann are of neuroblastic origin and that any tumor arising from the sheath is a neuroma. If this is true, we would be forced to include many of the tumors encountered in von Recklinghausen's disease and could find an explanation of the origin of our

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8. Stout, A. P.: A Tumor of the Ulnar Nerve, *Med. & Surg. Rep. Presbyterian Hosp.*, New York, 1918, vol. 10.

There was a mass which extended up to the middle of the scar and downward at least  $1\frac{1}{2}$  inches below the head of the radius. The mass seemed to be on the outer side of the biceps insertion. The skin moved freely over it. This mass was nodular, not painful and was movable in a lateral direction. Pressure on the mass did not produce any disturbance in the peripheral distribution of any of the main branches of the brachial artery. Apparently this mass did not have any deep attachment. Just above the external condyle and to the outer side of the triceps, there was a small nodular, firm mass which was not movable. The skin glided freely over the mass. I could not feel any axillary mass.

The patient was advised to have a roentgenogram of the chest made at once with the view of determining the operability.

He did not return until Dec. 31, 1926. At that time the following examination was made: On the outer side of the left elbow just lateral to the scar, the skin

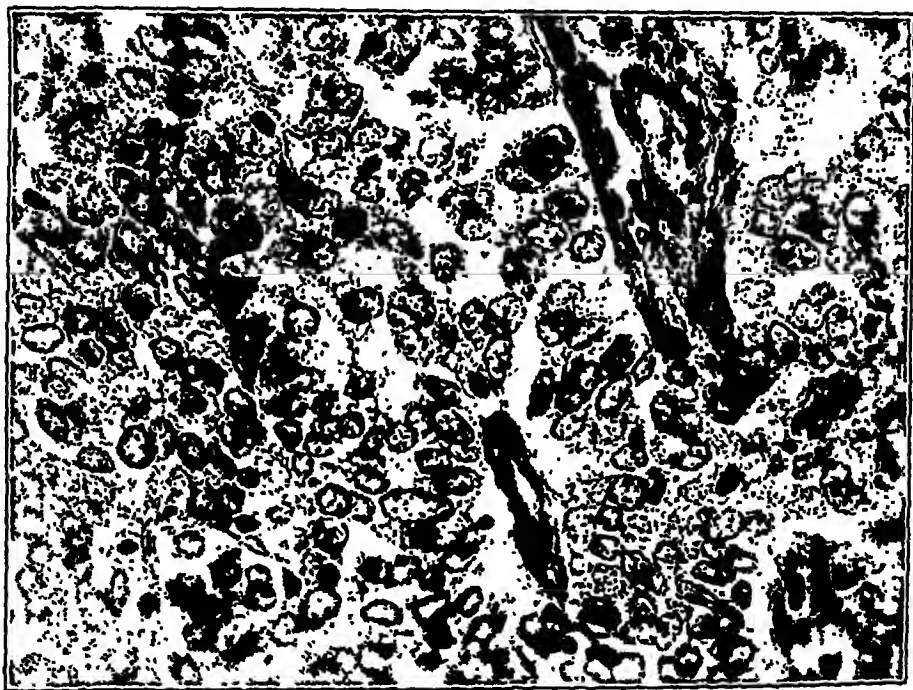


Fig. 23.—High power magnification of tumor in kidney.

had a bluish tinge. There was an irregular, nodular mass under this area. The level of the growth was four fingerbreadths below the external condyle and apparently under the supinator longus muscle. The upper limit of the mass was more than four fingerbreadths above the external condyle. The mass was movable in a lateral direction, but not up and down. The anteroposterior diameter of the mass above the elbow was about 2 inches. It was nodular, hard and painful. The mass extended upward along the upper border of the external condylar ridge of the humerus. There was limitation of extension of the arm, about 150 degrees, and flexion of 45 degrees. He was able to palmarflex and dorsiflex the wrist. Supination and pronation of the forearm were not impaired.

On the inner border of the biceps muscle, corresponding to about the middle of the arm in the course of the median nerve and brachial artery, there was a hard, nodular mass which was movable in a lateral direction, which was not movable up or down. It was not fluctuant. The size could not be diminished by pressure, proving that it was not a vascular dilatation, at least to my mind. Pres-



I can do no more than to leave this interesting tumor for further study by pathologists (Dr. Lanford and others) that it may eventually be properly catalogued.

*Summary.*—1. Recent investigations in embryology, particularly the work of Harrison, indicate that the sheath of Schwann is ectodermal in origin.

2. The clinical experience of Verocay and others indicate that neoplasms of the peripheral nerve arise from the cells of the sheath of Schwann.

3. These tumors of the peripheral nerve may be a part of systemic disease.

4. Recklinghausen's disease is not mesodermal in origin.

5. Penfield's work would indicate that he is in accord with these statements.

6. Epithelial neoplasms of peripheral nerves, when part of a systemic disease, may recur in the remains of the nerve, but they do not cause involvement of the lymphatics.

7. If recurrence occurs, amputation may be the only means of cure.

8. I believe that this tumor had its origin in the cells of the sheath of Schwann.

#### EPITHELIAL NEOPLASM OF THE RADIAL NERVE ASSOCIATED WITH NEOPLASMS OF LUNG, HEART, LIVER, BRAIN, DURA, CALVARIUM AND SUPRARENALS

*CASE 2.—History.*—Mr. J. J. G., aged 53, complained of symptoms which began in June, 1926, when he first noticed a hard lump in the "crease of the right elbow," which increased in size. On October 22, under local anesthesia a portion of the mass was removed by Dr. Metz. The mass recurred and became larger than before. He experienced pain, but function was not disturbed.

In March, 1926, he was told that he had tuberculosis, because of a cough and a purulent expectoration which was streaked with blood.

*Examination.*—Examination was made on Dec. 13, 1926. There was a scar about  $2\frac{3}{4}$  inches long on the lateral aspect of the right elbow. The skin on either side of this scar presented nothing of note. The right elbow was larger than the left elbow. There was apparently a diminished carrying angle and fulness in the antecubital fossa. The difference in size of the two forearms extended down to the wrist. The hand, on the palmar aspect, seemed slightly purple, in fact, the whole hand presented a mild cyanotic hue. When asked to pronate the forearm, he lifted the palm of the right hand up with the left; he called my attention to the fact that he was able to pronate the hand without the aid of the opposite hand, and demonstrated that fact.

There was tenderness and a noticeable difference in the size of all of the fingers, those of the right hand being slightly larger than the left. The muscles of the forearm were flaccid. The skin showed no difference in temperature. Palpation revealed all sensations present.



A circular type of incision was made. When the cuff of skin was retracted upward, the brachial artery was ligated. The axillary vessels were ligated. The median, ulnar and musculocutaneous nerves were cut high, and they were then "fish-tailed."

After this, the muscles were cut above, 1 inch higher than the skin cuff, the bone sectioned higher and the tourniquet released. Bleeding was not encountered. The muscles were quilted over, and the skin closed with interrupted dermol and fine continuous lock stitch.

The specimen was sent to the pathological department for inspection, section and dissection, and the following pathologic report was made: The axillary vessels lay on top of the median nerve and were closely adherent to the nerve. There was a groove on the inner aspect of this tumor mass made by the vessels. The median nerve could be dissected practically free from both vessels and the



Fig. 25.—Suprarenal gland, low power magnification of tumor.

tumor. The tumor mass measured 3 by 1.5 by 1 cm. It was irregular and nodular. In places, it seemed to have broken through its capsule and was adherent to the surrounding tissue. On the outer side of the growth and overlying it was a large nerve trunk mass. Peripheral branches of the nerve were seen coming out of the lower nerve of the tumor mass. Along the vessel which accompanied the radial nerve small but similar masses were found. The wall of the vessel at this point seemed thicker as though it contained some new growth. There was a mass lying under the supinator longus muscle, which was about 6 by 3.5 by 2 cm. The upper portion of the muscle was normal in appearance, but the mass seemed to have invaded it. It was nodular and grayish. The radial nerve was dissected down and followed into the growth. Above the level of its penetration there was a small nodule; this mass seemed to be of the same character as the rest. The radial nerve below the muscle was dissected down to the wrist and was seen emerging from the mass, while the nerve itself was smaller than expected normally. The supinator longus was sectioned in its most prominent point and

sure over this mass did not produce any disturbance in the peripheral distribution of the median nerve. Palpation in the axilla did not reveal any mass.

He was advised that "nothing short of a high amputation is going to be of any service."

*Progress Notes.*—Jan. 1, 1927: The patient was admitted to hospital for observation. The mass on the right arm, along the course of the radial nerve, was probably a malignant tumor of the nerve. He had a cough and raised bloody sputum. A roentgenogram of the chest was taken.



Fig. 24.—Liver showing metastatic tumor.

January 2: Roentgen-ray examination showed what was taken to be fluid in the right side of the chest with some pleural thickening.

January 3: An operation was performed. A diagnosis was made of recurring and metastasizing epithelial neoplasm of musculospiral nerve; metastasis had occurred to the median nerve.

The radiologist reported that "there was no evidence of metastasis to the chest."

Operation: The arm was amputated. Wyeth pins were introduced in the front and the back and in the upper limit of the axilla, and a rubber tube tourniquet was used.

January 9: Hemoptysis occurred again in the afternoon. There apparently was an ounce of blood.

January 10: The dressing was changed in the morning. The patient still complained of some pain. A small amount of blood was present in the sputum throughout the day. The patient said that the lump in the top of his scalp was larger.

A consultation with Dr. Lemann, chief of the medical service, was asked. He reported "It is my impression that there is fluid in the pleural sac and I would recommend exploration with a syringe. In spite of suggestive history of preceding tuberculosis, I am inclined to believe we are dealing with a pulmonary metastasis."

January 11: A laboratory report showed that the sputum was examined twice; tubercle bacilli were not found, but gross blood appeared both times.

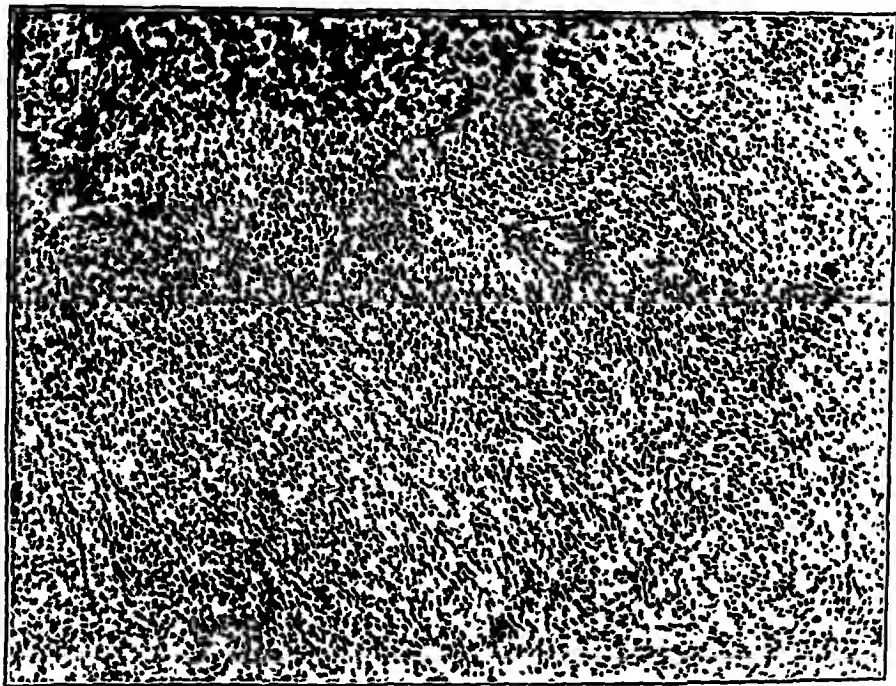


Fig. 27.—Tumor of spinal accessory nerve; low power magnification.

January 12: Profuse hemoptysis occurred in the morning. One-quarter grain (0.016 Gm.) of morphine was given twice, and 5 cc. of 10 per cent calcium chloride given intravenously.

January 13: The patient spat a little blood in the evening, for which morphine was given with good results; 5 cc. of calcium chloride was given intravenously.

January 14: The patient spat blood; 5 cc. of 10 per cent calcium chloride was given intravenously in the evening.

January 15: He did not spit blood. The dressings were changed and the sutures removed. The wound healed, with primary union. Five cubic centimeters of 10 per cent of calcium chloride was administered intravenously.

January 17: He had been spitting blood-streaked sputum the day before but morphine was not given. Five cubic centimeters of 10 per cent calcium chloride was given on that day and 5 cc. calcium chloride the following day.

January 18: The sputum was still streaked with blood.

January 19: The wound was dressed, and the patient allowed to go home, improved.

the tumor mass exposed. The cut surface varied from pink to gray and was rather uniform, with the exception of a number of areas of small yellow comedones that exuded on slight pressure. The under portion of the cut sections showed rather distinct lobulations, especially where they had encroached on and distended the muscle. Blood vessels were not a prominent feature. There was an irregular and nodular mass, measuring 7 by 5 by 2.5 cm. which sprang upward on the lateral side of the triceps tendon. When cut, it presented exactly the same appearance as the outer tumor.

A section was taken from the neoplasm involving the supinator longus, triceps and in the bicipital groove epithelial neoplasm presenting islands of embryonal cells, the centers of which showed keratinization. The young cells were somewhat columnar, and a few groups showing a suggestion of glandular arrangement surrounding new growth was suggestive of glia tissue (Lanford).

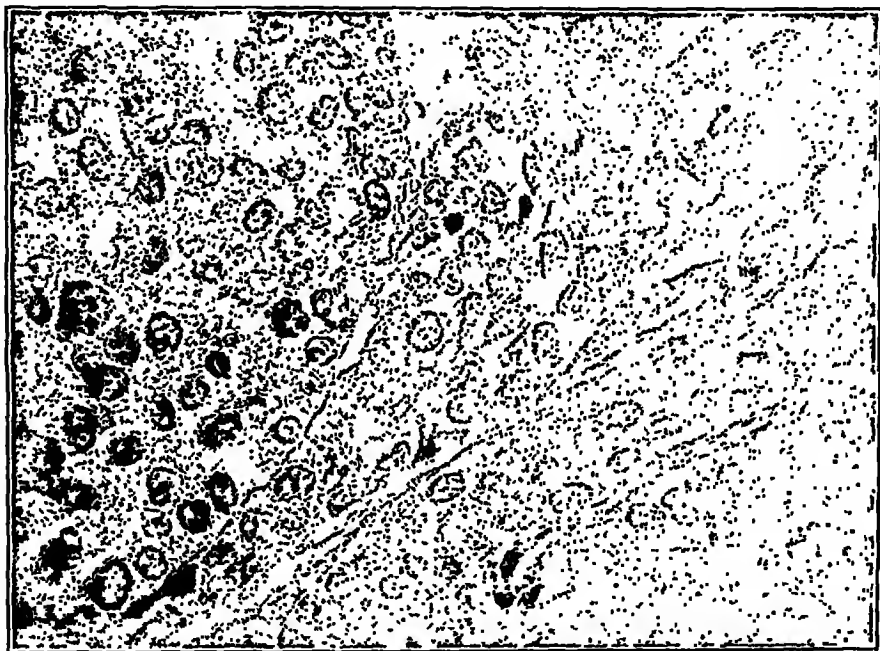


Fig. 26.—High power magnification of tumor of suprarenal gland.

On January 3, the roentgen-ray report stated that the left side of the diaphragm was smoothly contoured, the right obliterated. No increase in the size of the cardiac or great shadows was visible. In the upper reaches of the left side of the chest, small fan-shaped density was observed which was considered to be suggestive of an early tuberculous lesion. The same type of fluffy shadow was visible in the upper right side of the chest, and the changes were scarcely sufficient to warrant a positive diagnosis. In the base of the right lung, the diaphragm was obliterated, and a definite, fairly large density was observed of the type commonly seen when fluid obliterates the base. The pulmonary changes were insufficient to form the basis for a positive diagnosis of tuberculosis, although this must be considered as probable, but a neoplasm producing fluid cannot be ruled out. Consultation with the clinician was requested (Henderson).

On January 7, in the afternoon, the patient spat up a large amount of bright red blood and blood-stained sputum throughout the night. Hemoptysis occurred in the morning.

There was some bulging of the right side of the chest and a flatness of the whole right side of the chest. Râles were not heard, and the respiratory sounds were clear. The voice sounds were transmitted, not distant, but, if anything, intensity was increased. At the base, the voice sounds were distant and there were no râles. The mass in the side had not increased in size. The patient continued to expectorate blood freely.

March 19: At 6 o'clock, the patient had a coarse tremor of the left arm, the left leg and the left side of the trunk. This coarse tremor was accompanied by a fibrillary tremor of the fingers of the left hand.

There was a decided deviation of the angle of the mouth to the right and also a widening of the left palpal fissure. The weakness of the whole left side seemed to be becoming more prominent.

March 20 to 24: The patient was unable to raise his left arm. If the arm was elevated and the supporting force removed, the patient's arm dropped to the bed. There was a coarse convulsive movement of the left side (upper and lower extremities). The right pupil was dilated. Respiration was irregular, and the pulse became markedly irregular. There was progressive difficulty in swallowing as well as progressive stupor.

March 24: The patient died.

*Autopsy Report.*—Postmortem examination was made on March 25. The body was that of a white man measuring about 170 cm. in length and weighing about 140 pounds (63.5 Kg.). The head was covered with a full suit of black hair. The right arm had been amputated at the shoulder joint, and the scar was well healed. There was a scar on the abdominal wall about 1 inch from the midline extending along the costal border for 3 inches. There was an irregularity in the scalp corresponding to a firm irregular tumor mass that had extended entirely across the skull from one temporal ridge to the other; it involved about one half of the parietal bone anteriorly and extended backward to the occipital ridge.

When the peritoneal cavity was opened the gallbladder was found adherent to the wall; a number of adhesions were also found between the liver and the diaphragm; these were firm, but fairly easily broken up. The liver extended about two fingerbreadths below the costal border. There was no evidence of inflammation of the general peritoneal cavity. The appendix was retrocecal and showed a number of old adhesions. The cecum was found to be slightly distended, and the transverse colon was very much so. There was a small band of adhesions which were firmly contracted and empty. The lesser peritoneal cavity was normal. The lymph nodes were not enlarged.

When the sternum was removed, it was found to be adherent on the right side to the underlying structures of the right pleural cavity. The left pleural cavity was completely obliterated by firm adhesions between the wall and the lungs.

When the heart was removed, a cellular mass was found in the posterior portion of the sac. This was particularly striking between the entrance of the inferior vena cava and the superior vena cava. The mass involved the right lung and almost completely obliterated it.

The heart was flabby in consistency and dilated. The outer surface was pinkish red, and on the right ventricle there was a large soldier's patch. An irregular nodular secondary neoplasm was noted in the wall of the left auricle and a similar nodule in the wall of the right auricle. The endocardium was smooth, there being nothing within to correspond to the new growth on the epicardium. The attached portion of the aorta was the seat of a rather

He returned on February 24 because of persistent headaches.

Examination showed a circumscribed, hard mass which was movable with the skin of the scalp.

On the right side of the abdomen on the outer border of the right rectus, there was a small circumscribed, hard, slight movable, painless mass about 1 inch (2.5 cm.) in diameter. This mass did not increase in size when the patient coughed, nor was it reducible into the abdomen. The patient was advised that it was impossible to tell the exact nature of the condition without operation. In view of the facts of his past history, I advised removal.

The wound on the stump was entirely healed. No mass was palpable in the stump. The skin over the axilla and the stump was freely movable. There was nothing to suggest a recurrence or metastasis of the axilla.

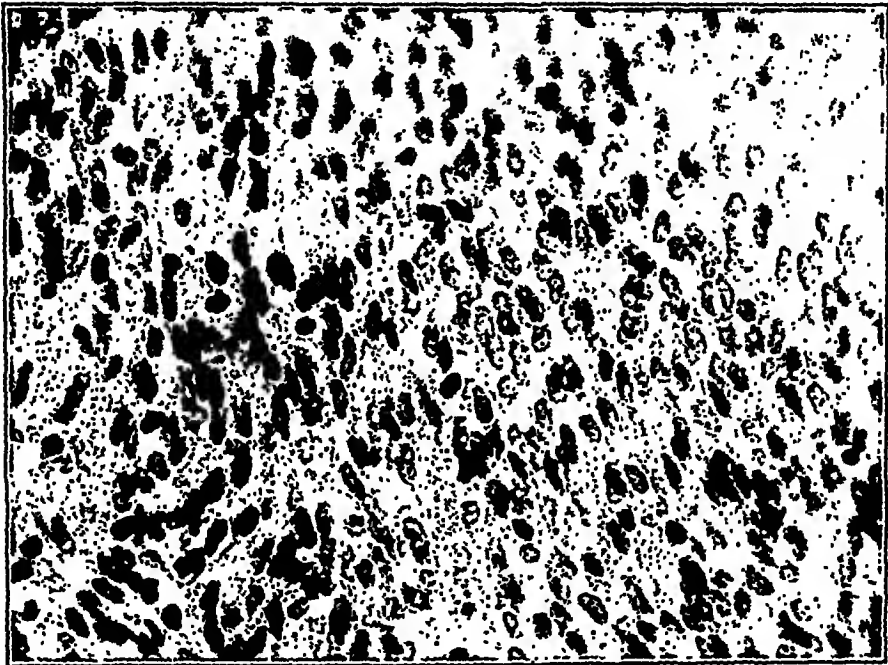


Fig. 28.—High power magnification of a tumor of the spinal accessory nerve.

*Second Operation.*—March 8, 1927: The preoperative diagnosis was tumor of the scalp and the abdomen. A diagnostic incision was made. In making preoperative diagnosis, the question arose as to whether we were dealing with metastasis from the original growth, or whether it was a cyst of the scalp.

An incision about 2 inches long was made over the most prominent portion of the tumor of the scalp. As soon as the skin had been reflected, we saw a solid tumor. We immediately realized that we were dealing with a malignant growth, and decided to remove a small portion for section. This was done and a specimen sent to the pathological department.

March 10: Since the operation, the patient had been restless and had complained that the weakness on the left side had been progressive. He lifted the left arm and forearm from the bed with difficulty. When the forearm was lifted up and the supporting force removed, the hand dropped. He had little grip. Loss of sensation in the distribution of the brachial plexus of the left side was noted.

was forcibly removed, it was found that the superior longitudinal sinus was free from involvement; the falx cerebri was also free of new growth. Sectioning of the brain showed the right cerebrum deeply infiltrated by the tumor mass for a distance of 1 inch in the middle portion of the parietal lobe and  $1\frac{1}{2}$  inches in the posterior portion; the new growth had extended over and pressed on the motor areas of the right side. The left side of the cerebrum was not infiltrated, the new growth being confined to the pia-arachnoid. The ventricles were normal.

The anatomic diagnosis was: carcinoma of the lungs and mediastinum; secondary carcinoma of the skull involving the dura; secondary carcinoma of the brain; secondary carcinoma of the kidney; secondary carcinoma of the liver; secondary carcinoma of the suprarenal; secondary carcinoma of the heart and pericardium; lobular pneumonia; chronic pleuritis; chronic splenitis; healed tuberculosis, pulmonary; toxic nephritis; dilatation of the heart, and acute splenitis.

The microscopic diagnosis was: squamous cell type carcinoma in the dura; brain, squamous cell type; in the suprarenal, secondary carcinoma with marked albuminous degeneration in the cortex; pancreas, normal; kidney, cloudy swelling, albuminous deposits and degeneration and chronic interstitial nephritis; spleen, chronic splenitis, passive congestion and amyloid deposits.

*Summary.*—1. This patient had a cough, hemoptysis and profuse purulent expectoration.

2. He had been treated for several months for tuberculosis.

3. He presented himself for examination after a tumor of the radial nerve had been excised.

4. The recurrent tumor at the original site was larger than the primary growth.

5. Roentgen-ray reports indicated fluid in the chest, without evidence of metastasis to the chest.

6. An amputation was performed.

7. A tumor of the scalp was later found to be malignant.

8. Prior to death, the patient developed progressive weakness of the left side of the body.

9. Autopsy revealed a carcinoma of the right lung, carcinoma of the skull, dura, brain, kidney, liver, suprarenal, heart and pericardium.

"All tumors resembled epithelioma, all, except the nerve tumor could be classified as carcinomata." (Lanford).

The difference between this and the first case is apparent.

Where was the original growth?

By searching the literature I found certain clues which may help to identify the present growth.

Is this a neurocytoma—neuroblastoma beginning in the suprarenals, or is it a metastatic carcinoma with the lung as the site of the primary tumor?

Like Marchand, it will have to be admitted at the outset that much that is hypothetical will have to be stated. If a mistake is made others will eventually correct our error.



early arteriosclerosis, small yellowish elevations being noted. The coronary vessels were markedly thickened, and in places, almost occluded.

The right lung was small and almost entirely obliterated by a new growth. The lower lobe was most involved. Attached to the lung and the bronchus, there was a large mass of lymph nodes which were almost entirely replaced by new growth. On section, the lobe was found to be practically destroyed and replaced by a cellular pinkish-gray structure containing a few areas of necrosis. The blood supply of the part was relatively scant. A small abscess cavity was found filled with pus. The upper lobe was the seat of many spots of new growth. The left lung was doughy and rather uniform throughout, no firm nodules being detected. In the apex, there was an area of tuberculosis, and posteriorly, an area of lobular pneumonia. A slight amount of fluid exuded on pressure.

The liver was slightly increased in size and relatively firm throughout. The dome on the right lobe, however, showed an area of increased consistency, but the outer surface over this area was smooth. In the lower portion of the left lobe, there was another area of increased consistency which had a rough and irregular outline and measured about 3.5 cm. in diameter. It was yellow. Throughout the entire anterior and superior surfaces of the liver were a number of tags of adhesions. On section, an enlarged tumor mass was found occupying the upper portion of the right lobe, measuring about 7 cm. in diameter. The tumor mass on section had a serrated irregular outline, and the cut surface was uniformly dirty yellow with a number of spots of necrosis.

The spleen was small and bound down by a few adhesions. It was flabby and slate gray, except a long irregular area of congestion across its anterior third. On sectioning, chronic splenitis was revealed, and some slight increase in the pulp was noted. Grossly, there was no secondary neoplasm.

The kidneys were slightly increased in size and rather flabby. They were more or less uniform throughout, except that in the left kidney there was a mass on its outer edge somewhat increased in density and oval in outline. On section, the entire cut surface was found rather uniform in appearance and presenting the picture of a toxic nephritis, and the area of increased density corresponding to a secondary growth. Several other areas of new growth were noted. The right kidney presented a similar picture but careful study failed to reveal any secondary neoplasm.

The right suprarenal was flabby, and an area of increased density was found, irregular in outline; on section this appeared to be a neoplasm. It was definitely within the border of the suprarenal and had destroyed it. The gross appearance of this new growth was the same as that of the new growth in the other organs. The left suprarenal was normal.

The testicle was free from a new growth. The bladder was filled with cloudy urine. The prostate was normal, and no evidence of neoplasm, either primary or secondary, was noted. The retroperitoneal space was free from any new growth. When the scalp was removed the tumor was found firmly adherent to and infiltrating the aponeurosis of the occipital frontalis muscle; palpation showed that it had destroyed the bones. The dura was firmly attached to the brain in the parietal portion by a tumor mass which had entirely infiltrated it. The tumor mass on its upper portion was rough, irregular, pinkish gray and contained spicules of bone by means of which it was continuous with the calvarium. There were several depressions in the superior surface of the external parietal lobe of the brain as a result of the new growth pressing down. The under surface of the brain was normal. The pituitary gland was somewhat swollen, but otherwise normal. When the dura



clinical and pathologic error in diagnosis, since the picture usually resembles some form of sarcoma and the tumor is as a rule diagnosed as such.

As Reisman points out, the failure to recognize the condition clinically may be due to the small size of the primary tumor, rendering it impalpable.

Meltzer<sup>12</sup> reported two cases:

**CASE 1. Clinical History.**—The patient, a man forty years of age complaining of severe stabbing pain in the left chest, shortness of breath, and cough. Roentgen-ray pictures showed opacity of the left lower chest to the level of the fourth rib anteriorly. A diagnosis of pleurisy with effusion was made.

**Autopsy:** The left lung was densely adherent to the chest wall, and when torn away no pus sac was discovered, but a great deal of degenerated, odorless material. This material came from the necrotic lower lobe, the greater part of which was occupied by a large tumor mass of a grayish color, with red and yellow patches of softening. This tumor measured 7 by 7 cm. in its greatest diameter. At the upper pole of the right kidney, just slightly invading the kidney substance was a rounded, firm, yellowish white mass, measuring 3.8 by 4 cm. Small portions of adrenal cortex were seen adhering to the tumor.

A soft hemorrhagic tumor, measuring 6 by 3½ cm. was discovered in the right frontal lobe.

**Microscopic examination:** The adrenal tumor consists essentially of diffuse deeply staining cells, interspersed here and there with bands of fine, pale, fibrils. The cells vary slightly in size, but the majority consists of a small dark rounded nucleus, with a very scanty cytoplasm in some, but in most no cytoplasm is evident. Other cells are pyramidal in shape with again practically no cytoplasm. Where the cells are crowded together densely the nuclei are elongated. Numerous mitoses are seen. A few very large cells, undergoing division, are present. The delicate fibrillar bands stain pink in eosin-hematoxylin sections. They do not possess the differential staining characteristic of neuroglia, fibroglia or collagen fibrils. The tumor is very vascular. Numerous thin-walled blood vessels are seen, and red blood cells lying free among the tumor cells. The "rosette" arrangement previously described is not observed.

In the lung tumor the same appearance is accurately reproduced.

**CASE 2. Clinical History.**—A man fifty-three years of age. Pain across upper abdomen, cough, and frequency of urination were complained of.

**Autopsy:** The body is that of a much wasted man with a very prominent abdomen. On opening the abdomen it is seen that practically the whole cavity is occupied by a hugely enlarged liver, which reaches to the right anterior superior spine. The liver weighs 11 pounds and is uniformly involved in a malignant process, being studded with tumor masses of varying size.

The right adrenal is of normal shape, but appears to be slightly enlarged. When cut into a small rounded tumor measuring 8 cm. in diameter is found to occupy the medulla. The cortex appears normal in the gross.

The lung is heavy and consolidated. The lower lobe is covered with a recent exudate. When the lung is opened a white mass 4 cm. in diameter and roughly spherical in shape is seen at the hilus. Several smaller white nodules are scattered throughout the lower lobe.

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12. Meltzer, Sara: Neuroblastoma Occurring in Adults, *Canad. M. J.* 16: 647 (June) 1926.

In 1910, J. Homer Wright<sup>10</sup> called attention to a group of tumors the nature of which has hitherto escaped general recognition. The essential cells of the tumor are considered to be more or less undifferentiated nerve cells or neurocytes or neuroblasts, and hence the names neurocytoma and neuroblastoma. They are considered to be neurocytes or neuroblasts for the following reasons:

1. The cells, at least in places, are associated with delicate fibrils, often of considerable length, which do not stain like neuroglia, collagen or fibroglia fibrils by Mallory's methods, and which are like the fibrils occurring in the "anlage" of the sympathetic nervous system.

2. The cells associated with these fibrils have the same morphology as the cells from which the sympathetic nervous system and the medulla of the adrenal develop, and which are regarded by embryologists as arising from migrated primitive nerve cells.

The fibrils may be arranged parallel to one another in bundles which are intimately associated with masses of the cells, as are the fibrils with the neurocytes in the "anlage" of the adrenal of a human fetus in the fourth or fifth month.

The tumors reported were found in the liver, lungs, adrenals, calvarium, brain and retroperitoneal tissue.

The occurrence of these tumors in such a variety of situations is accounted for not only by metastasis but also by the generally accepted teaching that undifferentiated nerve cells migrate from the embryonic central nervous system to form the nerves and ganglia as well as the sympathetic system.

Moreover, it seems reasonable to believe that certain other small cell tumors without the characteristic fibrils, occurring in various situations, are also of this nature.

Lederer<sup>11</sup> reported a case in 1926, which he classified as a neuroblastoma of the suprarenal gland. R. S., a girl, aged 4½ years, two months before admission had a swelling which appeared on the left side of the head and the left eye became prominent. At autopsy, a tumor involving the left suprarenal was found.

The cranial bones were involved. Tumors in this region "were of an osteoclastic nature as evidenced by a cellular invasion and osseous absorption."

In discussing the case he said:

In the primary tumor the ganglion cells were in parts of the tumor, being present in groups, or scattered singly among the spindle cells. In the metastases, however, after careful and prolonged search, no ganglion cells could be discovered. This corresponds to the observations of most authors that these tumors metastasize only by virtue of the undifferentiated cells. The absence of differentiated cells in the metastases is the chief reason for both

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10. Wright, Homer, J.: Neurocytoma or Neuroblastoma: A Kind of Tumor Not Generally Recognized, *J. Exper. Med.* July, 1910, vol. 12.

11. Lederer, Max: Neuroblastoma of the Adrenal Gland (Hutchinson Type): Report of a Case, *J. Cancer Research*, 1926, vol. 10.

fibrils or fibrous tissue. Comparing these neoplastic cells with the normal small round mono-nucleated cell, they were larger and more irregular in size and shape. The neoplasm was extremely vascular.

He summarized his observations and his study of the literature as follows:

As regards the occurrence of these tumors in such varied positions, this can be explained by the fact that the primitive nerve cells wander out from the embryonic central nervous system to form the sympathetic nervous system, and consequently tumors of this type may be found almost anywhere.

Finally, neuroblastoma may not be as rare as they were originally considered to be, as many which were or are diagnosed as sarcomata are really of nervous tissue. Of the two types neuroblastoma and ganglio-neuroma, the latter is the rarer of the two.

Of late years the interpretation of tumors of the nervous system has undergone many changes. For example, some years ago, the present case would have been classified as a sarcoma of the small round-cell type, but now it is recognized that neoplasms of the nervous system may be composed of the developing cells of the various parts of the nervous system. The neuroglia, or its various modifications may form tumors; as can also ganglion cells with nerve fibers, or the comparatively undifferentiated cell, which is the antecedent of these tissues. Thus we find tumors composed of cells which are the forbears of the sympathetic system, the chromaffin system, and the ganglion cells or neuroglial cells.

In the formation of the nervous system the epiblastic cells which line the medullary groove can develop into nervous elements or the supporting glial tissue. Nerve fibers may grow out from this central region and form the peripheral nervous system, or on the other hand neuro-epithelial cells may wander into the body and organs, and in relation to these organs give rise to the elements composing the sympathetic system.

In 1914, H. R. Wahl<sup>14</sup> reviewed the subject of neuroblastoma. He reported:

It is becoming recognized, especially in the last four or five years, that the most highly differentiated tissue of the body—the nerve tissue—may and does frequently undergo blastomatous change. True nerve tumors, i. e., growths consisting of specific nerve elements, may occur in any part of the nervous structure, but by far the greater number of them have their origin in the sympathetic system. These tumors may be either benign or malignant.

In his summary and conclusion, he stated:

Nerve tissue may give rise to new growths, which are properly called neuroblastoma.

Neuroblastomata are manifestations of a pathologic condition more or less localized or diffused in the whole or part of the nervous system. If localized to one focus, as is usually the case, the result is a solitary nerve tumor (ganglioneuroma); if generalized, multiple tumors result.

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14. Wahl, H. R.: Neuroblastoma, with a Study of a Case Illustrating the Three Types That Arise from the Sympathetic System, *J. M. Research*, 1914, June, vol. 30.

**Summary:** Neuroblastoma is a tumor almost confined to infancy, and early childhood. Both of the cases recorded in this paper occurred in adults.

In the microscopic picture one feature common to both tumors is the absence of "rosettes." We know that in the development of the sympathetic system the cells are frequently found arranged in rosette form. In the fully developed adrenal medulla these do not occur. This raises the possibility of some relationship between the age of the patient, and the finding of "rosettes" in the microscopic structure.

As the tumor is derived from the primitive nerve cell or neuroblast it may occur in any situation where such cells are encountered. It is, however, confined almost entirely to the sympathetic nervous system, and occurs most frequently in the medulla of the adrenal which itself is derived from that system.

It was pointed out some years ago by Frew that the site of the metastases depends on whether they are derived from the right or left adrenal. Thus if the primary tumor occurs in the left adrenal metastases will appear most frequently in the bones, especially the calvarium, but also in the liver and other organs, thus giving the first clinical variety. If the tumor is derived from the right adrenal, secondaries occur in the upper surface of the liver, the lung, and more rarely in the calvarium, and these fall into the second clinical group. We see that secondary growths occur most frequently in the skull, liver, and lungs, but they also occur in any of the bones, the sternum, vertebrae, ribs, and long bones: in the opposite adrenal, in the kidneys and even in the skin.

Apart from its position there is nothing characteristic in the gross appearances of a neuroblastoma. Microscopic, however, it possesses certain definite characteristics and a typical case can be recognized without difficulty.

Flemming and Davidson<sup>13</sup> reported a case in a boy, aged 4 years. The autopsy observations were:

The whole of the subcutaneous tissue of the scalp was replaced by a red fleshy mass of tumor growth. This growth covered the whole of the frontal, parietal, occipital, sphenoidal and part of each temporal bone on either side. It was dark red in color and had the appearance and consistency of muscle. Over the parietal bone the neoplastic mass was 1.5 cm. in thickness.

On section of the skull, the neoplastic growth was seen to penetrate the bone, so that most of the extradural space was occupied by a mass of malignant growth. There was very marked invasion of the internal surface of the frontal bone.

**Suprarenal Glands.** The left suprarenal was replaced by a large homogeneous, dark red, comparatively soft mass, 6 by 5.5 cm. in size.

**Long Bones.** Both those of the upper and lower limbs were definitely involved. The marrow was almost entirely replaced by tumor growth which invaded the bone, making it extremely friable and thin.

**Microscopic Appearances—Primary Neoplasm.** The tumor was composed of small cells which were either roundish or elongated in shape. There was very little cytoplasm present, the most of the cell being occupied by a nucleus which in many cases was hyperchromatic. In certain areas these cells tended to assume a "rosette" or circular formation. Interspersed among the cells was a meshwork of fine fibrils which did not stain with the specific stain for glial

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13. Fleming, Robert A., and Davidson, James: A Case of Neuroblastoma (Neurocytoma), *Tr. Medico-Chir. Soc., Edinburgh*. 1924-1925, pp. 142-151.

Whether this is a neurocytoma or neuroblastoma of the variety described by J. Homer Wright or whether it is a metastatic carcinoma with the lung as the site of the primary lesion, cannot be definitely stated at this time.

Neoplasms of the peripheral nerves associated with evidence of pulmonary lesions should certainly direct attention to the lung as a factor before operative intervention is resorted to.

The recognition that true tumors of the nerve, either benign or malignant, do occur in any part of the nervous system should be more generally appreciated.

#### ENCAPSULATED TUMOR OF THE SPINAL ACCESSORY NERVE

Solitary neoplasms of cranial nerves must be considered when differentiating masses in the neck. This single point is my reason for adding the third case to this presentation.

CASE 3.—Mrs. G. L., aged 53, was referred by Dr. I. I. Lemann because of the presence of a swelling on the right side of her neck. This swelling had been noticed only two months before she came under observation. There was a history that the mass increased and diminished in size. She complained that the mouth was dry and that recently there had been a small amount of saliva. Pain was not associated with the mass.

This patient had been under Dr. Lemann's care because of hypertension.

Tonsillectomy had been performed by Dr. R. C. Lynch one and one-half years before the present examination. Following the operation, there was a secondary hemorrhage which was controlled by sutures.

*Examination.*—She was examined on April 29, 1927. There was swelling on the right side of the neck which extended down to the upper level of the thyroid cartilage. The mass lifted up the sternomastoid muscle and seemed to extend upward to the tip of the mastoid. The skin over it was neither red nor glossy. Pulsation was not noted in the mass. There was a pulsation below the level of the mass, and this pulsation seemed to extend upward from the junction of the middle of the upper third of the clavicle and reached the sternomastoid about its middle posteriorly. A pulsation was noted in front of the mass, and this corresponded to the facial artery.

No palpable mass was found about the ascending ramus of the mandible on the right side. When the patient opened and closed her mouth, the condyle immediately under the skin could be palpated. The glands in the digastric triangle on both sides were palpable. There was a mass, the lower limit of which corresponded to the upper limit of the thyroid cartilage, which could be palpated as high, I believe, as the tip of the mastoid. The mass was not adherent to the muscles and could be moved laterally. It was not nodular, but seemed to be smooth. No pulsation was imparted to the finger. I could get a lateral range of motion of about 1 inch. The floor of the mouth did not show bulging, and with the finger in the mouth I could feel a mass lying immediately on top of what I believed to be the internal carotid artery. The mass did not cause any bulging of the posterior pharyngeal wall. There was no bruit over the mass.

The diagnosis was probable tumor of the carotid body.

Owing to the extensive variation in the degree of differentiation of the cellular and fibrillar structures in the undifferentiated type of nerve tumors different portions of a malignant neuroblastoma may differ widely in their appearance.

The possibility that this case represents metastatic carcinomas with the lung as the site of the primary growth cannot be overlooked.

Reference to Barron's excellent work on carcinoma of the lung is convincing. He stated:

The metastases from lung carcinomas are frequent and numerous. According to Adler, the principal metastases in his collection of 374 cases were to these organs: (1) lymph nodes, 117; (2) liver, 103; (3) lungs, 66; (4) kidneys, 58; (5) suprarenals, 38; (6) brain, 28 (dura mater, 10), and (7) bones (vertebrae, 5).

Briese, in his series of sixty cases, found metastases absent in only four cases. Of the twenty-one organs and tissues listed in the order of frequency, the principal ones involved were: (1) regional lymph nodes, 43; (2) liver, 25; (3) pleura, 17; (4) kidney, 17; (7) lungs, 11; (8) brain, 11; (9) bones, 9; (12) ovary, 7; (13) suprarenals, 6 and (17) dura, 3.

It is true that none of his collected cases present evidence of metastases to peripheral nerves, but there is evidence of metastases to the brain and spinal cord.

The other organs involved in our case are frequently involved in cases cited (liver and suprarenals).

Brunn stated:<sup>15</sup>

Metastases occurred in 85 per cent of the cases. Many of the initial symptoms were due to metastatic involvement. These occur relatively early and may be the condition that brings the patient to the doctor. A great many of the clinical diagnoses were made on metastatic involvement, mainly cerebral or bone involvement. The brain was involved in 12 per cent of the cases, the liver in 30 per cent, and the kidneys in 20 per cent. Two striking features in the occurrence of metastases are that the heart was involved in 21 per cent of the cases and the suprarenals in 14 per cent in a study of 626 case reports.

Lanford stated specifically that all of the growths may be considered metastatic carcinoma, except those of the nerve.

We know this patient had evidence of lung involvement before the tumor of the nerve appeared. Reference to his history shows that he was treated for tuberculosis long before he came under our observation. This is a common error.

*Summary.*—My second case illustrates a type of malignant epithelial neoplasm which not only recurs in the original nerve, but which may involve other peripheral nerves.

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15. Brunn, Harold: Primary Carcinoma of the Lung. *Arch. Surg.* 12:406 (Jan.) 1926.

running across it, giving the appearance of a myxomatous tumor. The cord previously mentioned looked like a nerve bundle.

*Progress Notes.*—Convalescence was uneventful except for slight parotitis. The wound healed primarily.

The laboratory examination (July 13) showed the specimen to be an irregular oval mass of tissue, measuring about 5 cm. in diameter, with a small projection about 0.5 cm. thick and apparently made up of a number of individual fibrils suggesting a nerve. The outer surface varied in color from a red to a yellow tinge, and the entire mass was pseudo-encapsulated. It was soft, but uniform. On section, it offered little resistance to the knife and presented a cut surface that varied from a light pearly gray to a pinkish tinge and was divided into irregular lobules by a connective tissue of increased consistency. The blood vessels were not prominent. Cellular neoplasm of undetermined type was diagnosed.

Microscopic examination showed that the specimen was made up of a number of cells occurring in irregular masses which were differentiating into nerve tissue. Some of the cells showed large vesicular nuclei, and in others, mitotic figures were present. The older cells showed a relatively well defined nuclei and a cytoplasm scanty for the most part and divided into innumerable little fibrils which were anastomosing with similar fibrils from other cells. The histology suggested glioma, whereas other areas suggested a more cellular form of neoplasm.

The diagnosis was neurocytoma (Lanford).

August 8: The examination following operation showed that the wound was entirely healed. There was no discharge. There was still some enlargement of the right side of the neck, and the skin was infiltrated. There were enlarged glands in the supraclavicular region. There was atrophy of the trapezius, supraspinous and infraspinous muscles of the right side.

The patient did not voluntarily completely extend the right elbow. The right shoulder was lower than the left. She volunteered the statement that she was unable to get her arm up to comb her hair.

August 10: She returned to the hospital, where 1,950 mg. hours of radium treatment was applied to the right side of the neck.

August 27: Atrophy of the muscles about the right shoulder was noted.

November 21: The right shoulder was much lower than the left. The clavicle was prominent, particularly near the acromioclavicular joint. There was a definite depression on either side of the clavicle at the outer end. Marked atrophy of the trapezius and supraspinous and infraspinous muscles was noted. Abduction of the arm was painful, and atrophy was more prominent when the arm was abducted.

Voluntary extension of the elbow was limited to about 150 degrees. Passive extension beyond that point was painful.

There was no limitation of rotation of the head. When the head was inclined to the left side, there was some discomfort as of stretching. No mass was palpable in the mouth.

The operative scar was smooth and freely movable. There was no palpable mass in the region of the previous tumor.

This tumor was solitary, encapsulated and developed along the course of one of the cranial nerves. For these reasons, it seemed to fall in the same class as neurinoma and acoustic neuroma. This classification is correct if the tumor arose from the sheath of Schwann, according to Verocay and Cushing.

Lanford's description would seem to place it in this category.

From my examination, I had the impression that it was a tumor of the carotid body for the following reasons:

There was a discrete, smooth, nonpulsating mass which had lateral mobility, but none in the long axis of the body. It was not adherent to the underlying structures. There was nothing which in any way would lead one to suspect aneurysm because of the absence of expansile pulsation and also because of the absence of bruit.

Primary carcinoma of the lymph glands of the neck is so rare as to rule it out ordinarily; more than that, the lack of fixation, the fact that the mass was discrete and that there were no similar masses seemed to eliminate carcinoma.

The blood dyscrasia seemed to be ruled out by the observations of Dr. Lemann. Cysts in the neck, branchial, thyroglossal, ranula were not usually found at this age. Aberrant thyroid must be considered, but the smooth, rounded contour seemed to eliminate that in my mind. Syphilis and tuberculosis seemed to rule themselves out on many grounds.

The diagnosis of tumor of the carotid body was made both by elimination and by the manifestations present.

The operation was not performed until July 13, 1927.

The preoperative diagnosis was undetermined, but several conditions were considered among which were a tumor of the carotid body, branchiogenic carcinoma, aberrant thyroid and possibly a cured false aneurysm.

An incision was made from the tip of the mastoid process, 3 inches in length, extending along the anterior border of the sternomastoid. The sternomastoid was reflected outward and the carotid vessels and jugular were exposed and retracted medially. The sternomastoid was lifted up, and the tumor could be palpated under it as far as the angle of the jaw.

The parotid gland was exposed at the upper angle of the incision. In order to have better exposure of the tumor, a second incision was made, beginning at the upper limit of the original and extending obliquely downward and backward along the mastoid process for about 2 inches.

The sternomastoid was cut across and reflected. This permitted us to obtain a free exposure of the mass. A tumor mass, about  $1\frac{1}{2}$  inches long and  $\frac{3}{4}$  of an inch wide was seen to occupy a position immediately lateral to the great vessels of the neck. The upper limit of the mass was continuous with a small "cord," the lower limit was continuous with a similar "cord" which extended down a short distance paralleling the vessels. The tumor itself, between the upper and lower structure, with which it fused gave the appearance of a punching bag suspended from a ceiling and held fast by an attached cord to the floor. The fibers of the cord above and below spread out over the bulbous enlargement like a fan. The upper portion of the cord could be followed upward under the mandible.

When an attempt was made to dissect the tumor away from this fanlike projection over its surface, we found that this was impossible.

The tumor was excised well above the upper limit of the bulbous enlargement and well below the bulbous enlargement. While we were removing the mass, that portion which had previously been described as being thin-walled ruptured, and a dark-yellowish material (which did not give the impression that it was gaseous) was spilled in the field. The mass was removed and turned over to the pathologist. All bleeding points were clamped and ligated, muscle planes approximated and skin closed. A gross section of the tissue showed a cavity with smooth, thick walls and many blood vessels



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Penfield<sup>16</sup> denies that this group arises from this source. He stated:

The fibers produced in these neoplasms show that the type cell bears no relation to neuroglia nor to the ectodermal sheath of Schwann cells.

Mallory (1920) in a careful histological study of the type cell of the so-called dural endothelioma suggested that the fibroblast was the type cell of the nerve sheath tumor as well as of the "endothelioma." He therefore proposed the name "peri-neurial fibroblastoma," assuming an origin from the connective tissue which surrounds the nerve. Inasmuch as we have found that the fibers in these tumors are not neuroglial and not nervous in nature but represent a particular form of collagen it is obvious that we must confirm Mallory's opinion provided the neurofibromata be excluded from the group.

The perineurial fibroblastoma must be considered to arise from the perineurial or endoneurial connective tissues which invests nerve fasciculi and fibers.

#### CONCLUSIONS

1. It may be presumptuous to attempt to classify this tumor in accordance with Verocay, Cushing and Lanford, in opposition to Mallory and Penfield; yet in view of the fact that I believe that the sheath of Schwann is ectodermal in origin and the fact that Lanford found cells which suggest "differentiation into nerve tissue," I believe that it is justifiable to consider this an epithelial neoplasm.

Future investigation may change the designation.

The essential points for us as surgeons are:

2. To recognize that solitary tumors of the nerve occurring in or on a peripheral or cranial nerve occur more frequently than we have accustomed ourselves to believe.

3. These tumors must be considered when masses in the neck are differentiated.

4. This tumor of the spinal accessory nerve was solitary. Up to the present time, the patient is comfortable, without any evidence of further trouble.

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16. Penfield, Wilder: The Encapsulated Tumors of the Nervous System. *Surg. Gynec. Obst.* **47**:178 (Aug.) 1927.

cause the injury that knife incision of the parenchyma would cause. Hemorrhage is avoided both during and after operation. Collective statistics on nephrolithotomy indicate that hemorrhage is usually frequent. At the International Urological Congress in Rome in 1924, collective statistics were given in 686 cases of nephrotomy; serious bleeding occurred in 85 (13.5 per cent) and 22 of the patients died.

If nephrectomy is indicated in cases of malignant tumor, tuberculosis or pyonephrosis, Rovsing begins by doubly tying the ureter with silk a few centimeters below the pelvis, and with cautery sears through the ureter slowly and cauterizes the mucous membrane in the lumen. Next, the kidney is isolated, care being taken that the capsule is not ruptured. The vessels are ligated with strong catgut and the kidney delivered through the wound. Then an incision 2 cm. long is made through the skin and fascia in the iliac fossa. A blunt perforation in the muscles and peritoneum is made and the peripheral stump of the ureter is drawn through and fixed to the skin. This guards against infection from the ureter, and in tuberculosis any subsequent tubercle of the ureter and bladder can be treated by the injection of a solution of carbolic acid.

Rovsing regards nephrectomy in polycystic kidney as inexcusable, even though some patients survive the operation. The disease is always bilateral and so little functioning renal tissue remains that uremia is not infrequently a sequel to the removal of one of the kidneys. It is essential to protect and set free as much as possible of the remaining kidney which is compressed by the tension of the cysts. This is done by multiple puncture of the exposed kidney which reduces it to normal size. The kidney is replaced and the wound closed around a drain. Oozing of urine or a chronic urinary fistula never occurs. Relapses are rare and renal function improves immediately after this type of conservative surgical procedure.

Rovsing uses a simple method of nephropexy which has the advantage over other methods of fixing the kidney securely in an absolutely normal anatomic position without injury, without leaving foreign bodies and without fixing the kidney to osseous structures. An angular incision is made, starting externally to the erector spinae muscle at the level of the tenth rib, passing perpendicularly down to midway between the twelfth rib and the iliac crest, and from there going forward for 10 cm. The kidney is drawn out through this incision, after being carefully loosened from its adhesions to the peritoneum and fat capsule. Retracted strands of fascia along the ureter are severed or loosened with a blunt instrument, as they tend to draw the kidney down again and cause pain. The membrane is incised longitudinally from the upper end to the juncture between the third and fourth quarters of the kidney, and from the ends of this incision, transverse ones are made out to the

## A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

E. STARR JUDD, M.D.

ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.

ROANOKE, VA.

GORDON S. FOULDS, M.D.

TORONTO

JEAN VERBRUGGE, M.D.

ANTWERP, BELGIUM

AND

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

### KIDNEY

*Surgical Technic.*—Rovsing<sup>1</sup> discusses his technic in operations on the kidney. The conditions most conducive to good results are the position of the patient and the incision which will give free access to the swollen, friable and adherent kidney. According to his procedure, the patient is placed on his back, in such a position that the edge of the table coincides with the free border of the erector spinae muscle, from which the lumbar region is readily accessible for the incision that begins midway between the twelfth rib and the iliac crest and continues forward to the border of the rectus muscle in cases of large tumor. In cases in which the ureter is to be exposed, the incision passes around the anterior superior spine of the ilium obliquely down toward the symphysis pubis. Through this incision, the hand may be introduced into the retroperitoneal space, and the kidney carefully and definitely isolated from its surroundings, thus bringing it uninjured outside the wound. This is important in ordinary suppurative processes, and in cases of tuberculosis and malignant tumors it is absolutely necessary in order to insure a good result.

In case a single stone lies free in an aseptic renal pelvis, Rovsing does not remove it through an incision in the pelvis. As a rule, he performs nephrolithotomy in the following manner: The stone is held between the thumb and index finger of the left hand, while an incision is made with a small knife in the capsule on the convex side of the kidney over the site of the stone. A forceps is then forced through the renal tissue on to the stone, dilating the opening so that a stone forceps may be inserted and the stone removed. This method does not

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1. Rovsing, N. T.: My Technic in Operations on Kidney. *Practitioner* 116: 164, 1927.

children. Mathé employs the silver wire method in opening the parenchyma of the kidney, and during the procedure he clamps the pedicle in order to lessen hemorrhage. He uses a double layer of mattress sutures to close the kidney. Fat is included in these sutures to prevent postoperative hemorrhage.

Phlebitis occurred in 2.8 per cent of Mathé's cases. It usually occurred in the internal saphenous vein. Treatment consisted of rest, compresses of hot boric acid and elevation of the affected member. Quinine, given either by mouth or intravenously, seemed to hasten recovery.

In thirty-two cases of nephrectomy for tuberculosis, the wound healed in the average time of ten weeks, and in nephrectomy for pyonephrosis, the average was three weeks.

Mathé pays careful attention to cardiac complications; in most of his cases the heart is examined by a competent internist before operation. Some patients are put on a digitalis regimen prior to surgical intervention. Mathé gives 15 drops of a digitalis product hypodermically every four hours after the operation until the pulse reaches 70. Although the peritoneum was opened on a number of occasions, symptoms of peritonitis did not develop. Usually, operations on the kidney can be performed extraperitoneally. In dissecting out large adherent tumors care should be taken not to injure the pleura. In case the pleura is injured, low-grade pleurisy develops, which usually clears up in a week or two.

In 50 cases in which operation was performed between 1906 and 1916, a period before complete urologic examinations were made, the mortality rate was 6 per cent. Between 1916 and 1926, the mortality was 2.04 per cent in 320 cases. A careful estimation of the renal function and a study of the working power of the opposite kidney allows elimination of cases with a poor risk.

Hinman, in discussing Mathé's paper, did not feel so confident about the safety of leaving clamps in place following nephrectomy, as Mathé has done in a number of cases. Hinman calls attention to a rather high percentage of fatal postoperative hemorrhages following release of the clamps, and he expresses the opinion that the clamps should not be left on except in extreme emergency. He has not left clamps on during the last ten years. He always carries out hypodermoclysis during the operation, so as to supply plenty of fluids to the patient before he recovers from the anesthetic. Hinman believes that a large proportion of failures in conservative as well as radical operations on the kidney are due to secondary infections. These infections are produced or made more serious by rough and prolonged operation. Dispatch at the time of operation is one of the greatest assets of successful renal surgical procedures.

sides. The membrane is then separated with the help of a flat sound, so that it looks like two folding doors or wings out to the sides. A strong piece of catgut is passed in and out through the portion of the membrane attached to the lower end of the kidney with a special needle curved on the flat plane. The ends of the catgut suture are next threaded through large curved needles and passed out through muscles and fascia to each side of the upper end of the lumbar incision. They are tightened until the kidney in the loop of catgut is drawn up into the exact normal position, and are tied over the fascia at the level of the tenth rib. The lumbar wound is sutured in four stages, the fascia and the skin with metal, and the muscle with catgut. After a period of from ten to fourteen days, the kidney is fixed in the normal position by the two wings of membrane. Rovsing has performed this operation about 300 times and considers it almost ideal. Pain entirely disappears, and in only 10 per cent of his cases has it partially returned.

Rovsing first performed nephrolysis in 1892, in a case of medical nephritis of the type which is now called nephrosis. Since then he has performed operations in at least 100 cases of nephritis that had been refractory to medical treatment, with an operative mortality of 4 per cent.

In cases of painful horseshoe kidneys without infection or other complications which would necessitate removal of one kidney, but in which it is simply a question of preserving all the renal tissue, Rovsing performs laparotomy through an incision in the rectus muscle, and exposes the isthmus by an incision in the posterior sheet of the peritoneum. The tissue of the isthmus is slowly crushed through with a powerful angiotribe until only the capsule persists. The angiotribe is removed and replaced by two narrow clamping forceps between which the capsule is cut through. The capsule is sewed close to the renal tissue with a continuous catgut suture, the forceps are taken off, and the liberated kidneys immediately retract into their respective beds. The two peritoneal wounds are carefully sutured and the abdominal incision closed.

*Surgical Complications.*—Mathé<sup>2</sup> reviews 370 cases of disease of the kidney in which operation had been performed in St. Mary's Hospital, San Francisco. The most common complications were shock, hemorrhage, cardiac lesions, phlebitis and embolus.

Surgical shock or exhaustion occurred most frequently in cases in which a considerable amount of blood had been lost after the removal of a large kidney. All bleeding points should be securely ligated during the operation. Loss of blood should be particularly guarded against in

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2. Mathé, C. P.: *Renal Surgery: Its Pitfalls and Complications*. California & West. Med. 28:57. 1928.

*Nephropexy.*—Petit,<sup>6</sup> who studied the late results in a series of cases in which nephropexy was performed during the last twelve years, concludes that this operation gives more lasting and better results in cases in which there is renal retention or persistent oliguria. The results are less satisfactory in cases in which nephropexy is performed because of pain in the region of the kidney without other urinary distress.

If patients are in pain because of a movable kidney, and are nervous and dyspeptic, signs of renal retention should always be investigated. This should be accomplished by means of ureteral catheterization.

If orthopedic or medical treatment does not relieve the patient, nephropexy should be performed because such kidneys usually contain fibrous or perinephritic lesions which diminish their functional value and predispose them to infection.

*Foreign Bodies.*—Brattstrom<sup>7</sup> reports a case in which two grass straws covered with concretions were found in the renal pelvis. The straws had probably been introduced through the urethra to the bladder and had found their way into the ureteral orifices and later the kidney. Nephrectomy was performed.

*Tuberculosis.*—Kidd<sup>8</sup> states that tuberculosis of the urogenital tract is a disease of adolescence, as common in males as in females, and induced by the stresses of puberty, work, marriage and parenthood. Clinical experience suggests that the human and bovine type of *Bacillus tuberculosis* produce two different types of disease. The first runs a rapid course and proves fatal in two or three years, a type which may be due to an infection with the human strain of the bacillus. The second runs a slow course of from ten to twenty years, in which the prognosis is excellent after surgical intervention, and in which the bovine type of bacillus may be concerned.

The bacillus is absorbed into the blood stream and may infect the kidney, seminal vesicle or testicle primarily, and no other organ of the body. In most cases, tuberculosis of the kidney appears as a unilateral blood borne infection. In women, the disease always starts in the substance of a kidney and extends into its pelvis, producing pyuria and increased frequency of urination. In men, the disease may start primarily in the testicle, extending along the lymphatics of the vas to the vesicle, prostate and base of the bladder, or it may start in both the testicle and the kidney.

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6. Petit: Les résultats lointains de la néphropexie, *Presse méd.* 2:1365, 1927.

7. Brattstrom, Erik: Unusual Case of Foreign Body in Kidney, *Acta chir. Scandinav.* 62:56, 1927.

8. Kidd, Frank: Treatment of Tuberculosis of Kidney, *Practitioner* 118:150, 1927.

Manson states that he agrees with Hinman concerning the leaving of clamps on the renal pedicle. If the clamps are left on, they should be removed with the greatest care by loosening a notch or two at a time for one or two days before complete removal. Too rapid or rough removal of a clamp may open up a vessel and start bleeding. Manson believes that the perirenal fat is frequently involved with the tuberculous kidneys, and should usually be removed also. He does not remove the ureter, but sutures it to the skin at the lower angle of the wound; in this way the wound does not break down.

*Renal Decapsulation.*—Molina<sup>3</sup> reports several cases of mercuric poisoning. One case was that of a young woman who had absorbed 2 Gm. of mercuric chloride. Various forms of medical treatment did not prevent the appearance of anuria. Bilateral decapsulation of the kidneys was performed thirty-six hours after the onset of anuria. The patient gradually recovered and passed a normal amount of urine. She was completely cured nineteen days after surgical intervention.

In comparing the surgical with the medical results, Molina agrees with Pousson, Legueu and Tisserand, that in cases of toxic nephritis, it is absolutely necessary to perform an operation as soon as anuria sets in. The operation, which should be performed quickly and without shock to the patient, does not cause disturbance of the renal function later.

[Ed. Note.—Quinby<sup>4</sup> reports a similar case in which decapsulation was performed for acute tubular nephritis from mercuric chloride poisoning. This patient was not benefited by the operation, and died five days after the onset.]

*Contusions.*—Klenka<sup>5</sup> reports three cases of wounds of the kidney. The first case was one of traumatic rupture of the kidney. Cure followed suture of the renal tear. In the second case, the upper third of the kidney had been torn away. Hematuria did not set in until seven days later. In this case, it was necessary to perform nephrectomy. In the third case (rupture of the kidney), the patient refused operation. For two months hematuria was intermittent and accompanied by fever. Nephrotomy was finally performed and a large perinephritic hematoma was found. The kidney was markedly congested but an outstanding tear was not found. Klenka believes that numerous fine lesions were present, but invisible macroscopically. The pressure of the hematoma against the kidney probably stopped the bleeding.

3. Molina, A. C.: Décapsulation du rein pour néphrite aiguë par intoxication mercurielle: un cas de guérison. *J. de chir.* 29:496, 1927.

4. Quinby, W. C.: A Note on the Results of Decapsulation of the Kidney for Various Forms of Nephritis. *J. Urol.* 13:321, 1925.

5. Klenka, Z.: Trois cas de plaies contuses du rein. *Bratisl. lekár. listy.* 6: 315, 1927.



1920, and details were obtained concerning 317. One hundred ninety-five of the patients (61.5 per cent) were cured; 28 (8.7 per cent) were not cured and 94 (29.9 per cent) died subsequent to the operation. One hundred and four of 125 patients operated on more than ten years previously were traced; 44 were dead; 58 (55.7 per cent) were cured and remained well.

Judd and Scholl report 863 nephrectomies: 611 patients were traced; 58 per cent were cured, and 31 per cent had died.

Wildbolz employs injections of tuberculin in many of his cases. The process of cure in these cases had been more certain and more rapid than in those in which tuberculin was not used. He believes that small doses of tuberculin are efficient. Small doses stimulate resistance, but large doses overwhelm and break down resistance. Kidd employs Koch's new tuberculin. Tuberculin should not be given until six weeks after an operation, and doses should be started with 0.00001 mg. If at the end of two years there are still traces of pus and bacilli in the urine, injections of tuberculin should be continued.

Thomson-Walker<sup>9</sup> states that renal tuberculosis is a disease of young adults, occurring most frequently between the ages of 20 and 40. It is rare in children, and is often bilateral in the early stages. In adults, chronic renal tuberculosis is unilateral in about 80 per cent of cases in the early stage.

Primary tuberculosis of the kidney rarely exists. A primary focus is always present elsewhere in the body, although it may not be discovered clinically. Coincident lesions were found by Braasch in 71 per cent of 346 surgical cases; they were noted by Persson in 50 per cent. In Thomson-Walker's cases, tuberculous lesions were noted elsewhere in the body in 40 per cent. In order of frequency, these extrarenal lesions are in the bones and joints and in the genital tract in the male. In Thomson-Walker's cases, there were tuberculous lesions in the epididymis in 23 per cent, in the prostate in 15 per cent and in the seminal vesicles in 7 per cent.

Miliary tuberculosis is usually an acute condition in which both kidneys are studded with tubercles. It is a part of general tuberculosis and is not of surgical interest.

Usually the first change takes place at the apex of a pyramid. Ulceration spreads outward toward the base of the pyramid, and a cavity communicating with the calix forms. Beyond this, there is a zone of inflammation which may show tubercles. Outward from this zone, isolated tubercles are scattered through the renal tissue. On the surface of the kidney, groups of tubercles are seen in areas corresponding to the subjacent tuberculous pyramids.

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9. Thomson-Walker, Sir John: *Tuberculosis of the Kidney*, Brit. M. J. 2: 625, 1927.

The most deceptive feature of tuberculosis of the kidney is the absence of pain in both kidneys until the later stages of the disease, and it is difficult to realize that one of the kidneys may be destroyed by the tuberculous process. The healthy kidney may ache at times because it is heavy, having increased to double its size in order to carry on the work of both kidneys.

In the more acute types, the onset of symptoms is an attack of profuse hematuria, which may be repeated once or twice. Pyuria is one of the most constant signs, but in chronic cases there are periods in which the pus disappears from the urine entirely, owing to ureteral obstruction. The general condition of the patient is usually satisfactory for the first year or two except in acute cases. There is no anemia or wasting, and there is no fever as long as the infection remains unmixed; later secondary infection from colon bacilli may occur which will induce fever.

In cases in which it is impossible to see the ureteral orifices, Kidd makes a small abdominal incision just below the umbilicus. Through this he inserts a gloved finger and palpates the ureters on each side as they cross the brim of the pelvis. If one ureter is thick and the other normal, and if the blood urea is within normal limits, he removes the kidney on the side of the thickened ureter.

Tuberculosis of the kidney inevitably leads to death after years of pain and misery unless the kidney is removed by operation. Early diagnosis, followed by nephrectomy, results in complete cure in at least 60 per cent of the patients so treated. In expert hands, due to the precision and accuracy of urologic diagnosis and surgical procedures, the mortality following operation should be less than 2 per cent. In 65 consecutive cases there were no deaths; the condition of 38 patients was observed until they were completely cured, in a number of instances from ten to fourteen years after operation. These data indicate that between 50 and 60 per cent of the patients should obtain permanent cure. Healing occurred by first intention in 36 of the 65 operations. Kidd removes not only the kidney, but the fatty capsule intact.

Legueu and Chevassu report 708 cases in which nephrectomy was performed for tuberculosis. Half of the patients were completely cured, one-fourth were improved, and one-fourth died within ten years after operation. They reviewed 638 cases in which the treatment was nonsurgical; 356 patients (51 per cent) died, mostly within from two to five years; 282 were alive, 22 more than ten years after the diagnosis had been made. They review data on 184 cases in which tuberculin was used; 51 of the patients were believed to have been cured.

Wildbolz performed an operation on 445 patients for renal tuberculosis; 11 (2.4 per cent) died within six weeks of heart lesions or embolism. Four hundred sixteen patients had been operated on before

In most cases the wound is closed without drainage. Drainage may be necessary on account of oozing or of infection of the perinephric tissues.

The operative mortality has fallen during the last twenty-five years. Recent statistics are satisfactory. In Thomson-Walker's 193 cases the mortality was 2.5 per cent. He was able to trace 111 of 188 surviving patients; 67 were well and without symptoms of urinary disease at periods of from one to twenty-two years after the operation; 25 were in good general health but still had symptoms. Of 19 patients who died after the operation, 11 (57.8 per cent) died during the first three years.

In none of Thomson-Walker's cases was cure obtained by tuberculin. Frequently symptoms were ameliorated and the general health improved for several years, but the tuberculous disease persisted. Tuberculosis of the kidney cannot be cured by exposure of the patient to sunlight; the temporary improvement that may take place encourages the patient to refuse operation or to postpone it. Heliotherapy is valuable after the operation; it is also useful in cases in which operation is contra-indicated.

In an inquiry among the physicians of Switzerland, Wildbolz found that of 316 patients suffering from renal tuberculosis and on whom operations were not performed, 31.3 per cent died within the first two years, and 27.2 per cent within from three to five years. More than half (58 per cent) died within the first five years, and only 20 per cent were alive after five years.

Fullerton<sup>10</sup> recently investigated a series of 158 cases of tuberculosis of the bladder that had been observed for several years. There was definite evidence of renal involvement in 141.

Fullerton's most successful operations were removal of the kidney and of as much of the ureter as could be reached through the lumbar wound. He did not find it necessary or desirable to dissect out the ureter. He believes that the removal of infected nodes surrounding the pedicle close to the spine is attended with risk. His present practice of dealing with the ureter at the point of section is to inject with a hypodermic syringe pure carbolic acid into the lumen for 2.5 cm. or more, before ligation and division of the ureter.

Nephrectomy was carried out in 73 of the cases; 6.8 per cent of the patients died as the result of operation. Fifty-five of the 68 surviving patients have been traced. Fifteen have died, 4 of them after long periods of complete relief. Forty-one patients not subjected to operation were traced; 26 (63 per cent) were dead.

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10. Fullerton, Andrew: Statistics of Post-Operative Survival in Renal Tuberculosis, *Brit. M. J.* 2:630, 1927.

Tuberculous lesions of the kidney may be arrested as the result of one of two processes: (1) healing of the tuberculous lesions with disappearance of the *Bacillus tuberculosis* and replacement of the ulcer with a scar, and (2) exclusion of the tuberculous focus by a ring of fibrous tissue. This may occur in three ways: tuberculous hydro-nephrosis, massive caseous tuberculosis of the kidney and occlusion of an ulcerocavernous focus.

The discovery of the bacillus of tuberculosis is the final proof of urinary tuberculosis. The bacillus was found in the urine in 85 per cent of Persson's cases, in 70 per cent of Beer's and in 90 per cent of Wildbolz'. In 193 cases in which Thomson-Walker performed nephrectomy for renal tuberculosis, the bacillus was found in 155 (80.3 per cent).

The modern treatment of renal tuberculosis is nephrectomy in all cases if the other kidney is healthy and there is no definite contraindication. This treatment is based on three postulates of the surgical pathology of chronic renal tuberculosis: (1) tuberculosis of the kidney is a progressive disease, (2) tuberculosis of the kidney is unilateral in the early stage and bilateral in the late stage, and (3) removal of the tuberculous kidney usually prevents infection of the other kidney.

The immediate postoperative mortality of nephrectomy in bilateral renal tuberculosis varies from 66 to 80 per cent and the benefits gained in the few surviving cases have not been permanent. The procedure is justified only in exceptional cases.

Various methods of dealing with the tuberculous ureter have been described: (1) the ureter is cut across below the kidney, the end seared with cautery or with pure carbolic acid and dropped back into the retroperitoneal space, and pure carbolic acid is injected into the ureter; (2) the ureter is cut across below the kidney and the end is sutured to the skin in the lumbar wound, or is brought up to the surface inside a drainage tube and fixed there; (3) the kidney and ureter are removed through a lumbar iliac incision (nephro-ureterectomy), and (4) the kidney is removed by the lumbar incision and the ureter cut across. A second small incision is made in the inguinal region through which the ureter is removed.

The method that Thomson-Walker uses is to remove the ureter as far as the brim of the pelvis through the lumbar wound, sear it with the cautery or with pure carbolic acid, apply a ligature, and drop it into the retroperitoneal space. The patient is reexamined in six months, and if there is reason to believe that the disease is still active in the ureter and is infecting the bladder, extraperitoneal ureterectomy is performed through a median suprapubic incision. The cases in which ureterectomy is advisable are those in which there is stricture at the lower end of the ureter and dilatation of the duct. The proportion of cases in which this is required does not exceed 8 per cent.

immediate intervention is urged. Interruption of pregnancy does not stop the tuberculous process, and this procedure is increasingly dangerous in later months.

Pugh unhesitatingly recommends nephrectomy in cases of renal tuberculosis in pregnant women. He examined the records of thirteen cases in which nephrectomy was performed by others. In eight cases, uninterrupted pregnancy and delivery at full term resulted. In four cases, abortion had to be resorted to after the nephrectomy. The diagnosis in the remaining case was vague. Of three patients observed by Pugh, two came to full term following nephrectomy. The uterus of the third was emptied at the fourth month, the patient dying one month later. Apparently pregnant women stand the operation well, and it is not more serious than when attempted in the nongravid state.

*Perirenal Hematoma.*—Hübner<sup>14</sup> states that clinical identification of perirenal hematoma was first described by Raye in 1839, and by Willis in 1841, and was called "apoplexia renum." Wunderlich later enhanced its clinical significance. There are many conjectures regarding the pathogenesis. There is no single explanation that covers all types of cases.

Perirenal bleeding does not always come from the kidney itself. Lâwen describes a hemorrhage from the iliac artery, which reached from the prostate to the diaphragm and encircled the kidney. A similar observation is made by Michaux following the spontaneous rupture of the epigastric artery. Not infrequently it is impossible to determine the source of the bleeding either by operation or necropsy; in one case, a massive hemorrhage was found in the renal region following scarlet fever. True perirenal bleeding is that coming from the kidney proper or the renal capsule, as well as those cases with blood between the fibrous capsule and surface of the kidney. These are more accurately designated as "perirenal hematomas," while massive hemorrhages are designated "retroperitoneal hematomas."

Chronic renal disorders have frequently been found associated with perirenal hematoma. The condition of the walls of the blood vessel and increased blood pressure have been thought to produce a hemorrhagic diathesis. Israel designates this as essential renal bleeding because of the absence of definite symptoms. Most authors, however, favor nephritis as the causative factor.

Hübner undertook some experimental work to determine the actual cause of the bleeding. He performed nephrotomy in some instances, and in others he clamped the renal pedicle, in periods varying from ten to thirty minutes, with the idea of creating a disturbance in the renal circulation. In most instances, definite subcapsular bleeding was noted.

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14. Hübner, A.: Das Perirenale Hämatom. Experimentellar Beitrag zur Frage der Genese, Arch. f. klin. Chir. 145:338, 1927.

Statistics support the contention that, with our present knowledge, operation remains the most hopeful method of treatment. If performed early, before deep ulceration has taken place in the bladder, relief is often immediate.

[ED. NOTE.—Various reports recently have suggested the necessity of surgical procedures in unilateral renal tuberculosis. Joly<sup>11</sup> states that urologists are unanimous in advising early operation. Joly quotes Rafin as saying that 91 of 168 patients not operated on were dead, the majority within the first three years after the onset of symptoms. In all, about 90 per cent of patients with renal tuberculosis who are not operated on die from the disease. Even patients who survive are rarely free from symptoms. Clinical cures are so rare that they do not appreciably influence the statistics. Israel states that a nonoperative cure for renal tuberculosis does not exist. The infection may be well localized and of low virulence, or the patient may, by reason of chronicity and numerous foci of infection, have acquired a tolerance and resistance to the bacillus. Braasch believes that immunity develops with multiplicity of lesions. In most cases, the infection destroys the kidney, spreads locally, extends to the bladder, and often causes disease of the other kidney. Nephrectomy is the operation of choice. Conservative surgical procedures are not practical in cases of tuberculous kidneys, and at best afford only temporary relief.

The statistics of Kümmell<sup>12</sup> concerning the spread and extension of the disease noted at necropsy in cases in which operation had not been performed, suggest the course usually taken by the disease when allowed to continue without surgical interference. In a review of 40,621 necropsies from the Eppendorfer Klinik, Kümmell gives 119 cases of tuberculosis of the kidney. In 84 of the cases, the condition was bilateral and in 35, unilateral. In contrast to this, bilateral infection was found in only 5 of 100 surgical cases of renal tuberculosis.

In the cases in which operation was not performed, there was evidence of other foci of tuberculosis in 99.2 per cent and in those in which operation was performed, 44 per cent.

Pugh<sup>13</sup> reviews the literature and records that in 69 per cent of cases in which exacerbation of unilateral tuberculosis occurred during pregnancy, abortion or nephrectomy became necessary immediately. Thus it would seem that pregnancy, instead of increasing the necessity for conservative treatment of renal tuberculosis, would contraindicate it. As the renal process is acutely exacerbated in 71.1 per cent of the cases.

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11. Joly, J. F.: The Late Results of Renal Tuberculosis, *Brit. J. Tuberc.* 19: 188, 1925.

12. Kümmell, H.: Ueber Nierentuberkulose, *Ztschr. f. Urol.* 17:18, 1923.

13. Pugh, W. S.: Tuberculosis of the Kidney in Pregnancy, *Ann. Surg.* 86: 591, 1927.

Nephrectomy is the procedure of choice, although in certain neglected cases preliminary incision and drainage may be indicated. Molesworth advocates preliminary laparotomy, and cites three cases of concurrent peritoneal injury in support of his views; in each of these cases, however, the kidney was removed and the rent in the peritoneum closed through an incision in the loin. In the presence of symptoms strongly suggestive of intraperitoneal injury, exploratory laparotomy is indicated, but if the abdominal contents are found to be uninjured, the wound should be closed and the kidney removed through an incision in the loin.

Analysis of the small series of recorded cases justifies the statement that with the wider application of instrumental diagnostic means, exploration of the abdomen will rarely be indicated in case of rupture of the sac, since, if the true nature of the injury is recognized, one can be reasonably sure that there are no complicating intraperitoneal injuries.

Papin<sup>17</sup> states that in surgical treatment of hydronephrosis, two extremes should be avoided, the essentially conservative and the radical. Conservative treatment was predominant in the earlier period of renal surgical procedures, and was replaced by radical treatment. Differentiation of the cases of hydronephrosis in which surgical treatment should be given and those in which medical treatment should be administered, can be determined only by pyelography. The old surgical procedures consisted of pyeloplicature and other plastic measures on the pelvis and ureter.

Nephropexy serves satisfactorily if the ureter is kinked and is unsatisfactory in cases with small congenital dilatations. The resection of anomalous arteries, which is similar to the so-called resection of Albarran, brings about atrophy of the corresponding renal segment.

Papin resected part of the renal pelvis in 6 cases; this was followed by renal drainage and nephropexy. In 2 cases he performed partial nephrotomy with dilatation and drainage of a large superior calix; in 1 case, partial resection of the kidney was performed and in another case pyelo-ureteral anastomosis.

*Ptoxis*.—Demel<sup>18</sup> reports his experience in 22 cases of nephroptosis. Operation was performed in 7 of these and there were 3 recurrences. In 1 of the 4 remaining cases a different pain developed, although the renal pain disappeared. The associated pain in 2 other definite cases of removable kidneys disappeared after appendectomy. The remaining 13 patients were not operated on. Seven of these were completely relieved by abdominal binders and 3 were greatly relieved by the wearing of supports.

17. Papin: Les opérations conservatrices dans les hydronephroses, *Presse méd.* 2:1365, 1927.

18. Demel, Rudolf: Ist die Nephroptose ein chirurgisches Leiden? *Beitr. z. klin. Chir.* 139:96, 1927.

It was believed that this was the result of stagnation of blood in dilated vessels and capillaries, thereby leading to bleeding by diapedesis. A series of experiments was also carried out to observe the influence of trauma, and it was concluded that the mechanism of hematoma is due to trauma and to hemorrhagic diapedesis.

*Hydronephrosis.*—Hellstrom<sup>15</sup> reports two cases of hydronephrosis in which the pelvic dilatation was probably caused by the oblique course through the wall of the pelvis of the upper end of the ureter.

Hellstrom recognizes three types of pathologic change at the ureteropelvic juncture: congenital preformations, inflammatory processes and mechanical change produced through irregular dilatations of the wall of the renal pelvis. In the two first types, therefore, the changes at the ureteropelvic juncture are the primary factors and the cause of hydronephrosis; in the third type the contrary is true. A combination of these three possibilities may occur naturally; it may then be difficult to determine which form is present. In one of Hellstrom's cases, the extrarenal portion of the renal pelvis was about 9 cm. in diameter. The ureter, which was not dilated, arose from the lower wall of the renal pelvis, curved sharply upward and was fixed for about 1 cm. to the anterior wall of the renal pelvis; from there it was unattached and turned downward in an acute angle. In the second case, the kidney was large, dilated and almost completely destroyed. The ureter started from the anterior and medial wall of the renal pelvis about 2 cm. from its lower pole and passed for a distance of about 1 cm. obliquely through the wall of the pelvis from below upward. In a third case, that of a large hydronephrotic sac, the obstruction was believed to have been caused by spastic conditions at the ureteropelvic juncture.

Herman,<sup>16</sup> in reporting a case of rupture of a hydronephrotic sac reviews the literature carefully. The condition is rare, from twenty-five to thirty cases only having been reported.

The case reported was that of a woman, aged 27, who was known to have pyelitis. She had been injured by a motor truck and was admitted to the hospital complaining of pain on the right side. There was tenderness and rigidity over the right flank. Signs of intra-abdominal injury were not present. The urine was bloody. A cystoscopic examination four days after the accident showed bleeding from the right kidney. A week later a pyelogram revealed rupture of a hydronephrotic sac on the right side. Nephrectomy was followed by recovery. Only two cases are on record in which a correct preoperative diagnosis was made.

15. Hellstrom, John: Contribution to the Knowledge of the Etiology of Hydronephrosis. *Acta chir. Scandinav.* 62:167, 1927.

16. Herman, L.: Case of Ruptured Hydronephrosis. *J. Urol.* 18:458, 1927



roentgen-ray opaque type of catheter is most satisfactory as it resists corrosion for a longer period than the ordinary plain catheter. He uses as large a catheter as possible with a large eye, cutting the meatus if necessary. The results are said to be better with the larger catheters. Pain, if it occurs from the indwelling catheter, is controlled by narcotics.

Corbus and Danforth,<sup>21</sup> in a study of pyelitis of pregnancy, find that although palliative and conservative measures afforded relief there was evidence of trouble persisting after delivery. In such cases treatment should be instituted after the pregnancy ends, in order, if possible, to restore adequate urinary drainage. In thirteen consecutive cases in which pyelographic studies were carried out after the termination of pregnancy, lesions were demonstrated in the urinary tract. Since lesions were present in the urinary tract after termination of pregnancy in all the cases studied, it seems reasonable to assume that they may have been present before the pregnancy began.

Crabtree<sup>22</sup> believes that there is a great deal that is not understood about the relationship of ureteral stricture to pyelitis of pregnancy. He is convinced that if stricture exists in many pregnant women with pyelonephritis, it is of only a few weeks' duration and that the patient recovers spontaneously after delivery. He does not think it is present in the majority of ureteral and pelvic dilatations in pregnancy. The return to normal of such kidneys without treatment for stricture is too rapid, and proper drainage measures will relieve the distention in the absence of ureteral dilatation. Crabtree recognizes that such a statement only adds to the controversy over the "clinical" stricture. In his clinic, he demonstrated in postpartum pyelonephritis an area of inflammatory change in one case sufficient to deform the course of the ureter. Stricture subsequently developed at that point. The severity of inflammatory reaction in the partially closed type of kidney found in the pregnant woman is favorable to the formation of stricture after delivery, on account of the scar tissue. In one case, a stricture developed within a year following pyelographic evidence of its absence.

The evidence available on the subject of the formation of the stricture in pyelonephritis of pregnancy is extremely meager. It is rarely possible to learn the condition of the urinary tract either before or early in pregnancy. Pyelography either during pregnancy or within three months following delivery is unreliable, since interpretations made on pyelograms taken before the kidney has recovered from the distention present during pregnancy are misleading. Different degrees of disten-

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21. Corbus, B. C., and Danforth, W. C.: Pyelitis in Pregnancy, *J. Urol.* 18: 543, 1927.

22. Crabtree, E. G.: Stricture Formation in Ureter Following Pyelonephritis of Pregnancy, *J. Urol.* 18:575, 1927.

Demel states that nephropexy should not be performed: (1) in cases in which the anatomic factors are not definitely explained, (2) in cases of generalized enteroptosis, (3) in cases of painless movable kidney; (4) in cases of gastro-intestinal symptoms or (5) if patients are hysterical or neuropathic. Usually nephropexy is not a satisfactory treatment for hydronephrosis associated with movable kidney. The operation should be undertaken only in cases of marked renal pain and distention which is caused by intermittent hydronephrosis or acute obstruction due to circulatory disturbances or kinking of the renal pedicle or of the ureter.

Demel believes that the conservative nonoperative treatment should be attempted usually, and that in most cases it will be successful or partially so.

*Pyelonephritis*.—Stephen,<sup>19</sup> in discussing pyelitis in children, states that simple bacilluria may exist without cells in the urine. It is difficult to recognize bacilluria without pyuria, and often there is a long course of illness before it is correctly diagnosed. *Bacillus coli-communis* is usually the cause of pyelitis; this term covers several species besides *Bacillus coli-communis* proper, such as lactose fermenters, *Bacillus cloacae* and the *Bacillus lactis-aerogenes* and the nonlactose fermenters, *Bacillus typhosus*, *Bacillus proteus*, Gärtner's bacillus and Morgan's bacillus.

One hundred and eleven of the 148 patients with pyelitis who were treated at the Royal Alexandria Hospital were females. The duration of pyrexia varied from eight to sixteen days. Treatment with alkalis for long periods was usually successful. Alternating the alkalis with methenamine and sodium acid phosphate has been advised, but Stephen obtains the best results by persisting in an uninterrupted course of alkalis.

Infants, 12 months of age, frequently required and tolerate 2 Gm. (30 grains) of sodium bicarbonate and 2 Gm. potassium or sodium citrate three or four times a day. Vaccine has often proved invaluable in the treatment of chronic pyelitis in children, but usually must be continued for several weeks.

If there is a history of definite pyelitis extending over a period of months, the patient should be referred to a urologist for pelvic lavage.

Pugh<sup>20</sup> has studied pyelitis of pregnancy and reviews the literature carefully. He believes that urinary antiseptics are of questionable value in this disease and says that treatment should be limited to the use of large draughts of water at frequent intervals. He advises the use of the indwelling catheter as the ideal form of treatment in all cases. The

19. Stephen, E. H. M.: Pyelitis in Children, M. J. Australia 2:142, 1927.

20. Pugh, W. S.: Pyelitis of Pregnancy; Its Treatment with Indwelling Catheter, J. Urol. 18:553, 1927.

He believes that if the patient is ill, drainage should be instituted, and the indwelling ureteral catheter gives the best results. In studying a large series of pyelograms, he has seen dilated calices and pelves which have made him consider the possibility of previous pyelonephritis, but the history did not confirm this; on further investigation, however, he has found this to be the result of previous pregnancies.

Kretschmer does not agree with Eisendrath as to the advisability of routine drainage in cases of acute pyelonephritis by means of the indwelling ureteral catheter. He does not use drainage in those cases except in pregnancy, and then not often.

Hooe states that he left the catheter in one side for eight days and in the other side fourteen days. Untoward results did not follow.

*Pyelovenous Back-Flow.*—Gile<sup>24</sup> reports a comprehensive group of experiments which he recently carried out in the hope of determining the mechanism of pyelovenous back-flow. In corrosion specimens of the renal pelvis of cadaveric specimens, venous outbranchings were not obtained except when extravasation had occurred.

The results from injections of dye were similar to those of Hinman; the venous system was injected regularly, the tubules were never more than partially injected and this rarely. Roentgen-ray observations of opaque solutions injected confirmed those made by Hinman. None of these observations, however, demonstrate how the substances reach the blood stream from the pelvis. Normally, there is no intrapelvic pressure. Under a positive pressure, there may be microscopic ruptures, filtration, osmosis, increased permeability of the pelvic membrane, lymphatic absorption or the opening up of a direct communication already present in the angles of the minor calices as suggested by Hinman.

The tubules are undoubtedly partially injected, but since dye is found in the blood vessels and not in the tubules following injection of living mammalian kidneys, it would seem that they are not significant in the production of back-flow.

The living kidney of the frog apparently presents a different mechanism, as in it the tubules were easily filled.

The term "pyelovenous back-flow" is illustrative, if it is understood in a general sense, of the passage of substances from the renal pelvis to the venous circulation. Probably this phenomenon does not occur by way of the tubules; its exact route has not yet been demonstrated.

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24. Gile, H. H.: Observations on Injections of the Renal Pelvis, *J. Urol.* 18:621, 1927.

tion of such pelves will give entirely different pictures. The slack following distention has not yet been considered.

Pugh has found that the stricture occurs in the ureter at points where there can be no pressure from the fetus; it is the result of inflammatory changes attendant on pyelonephritis of pregnancy. It is noteworthy that the few strictures which have been observed in the pregnant women of his clinic did not cause symptoms immediately after delivery but months afterward.

Eisendrath<sup>28</sup> makes a plea for the more widespread use of the inlying ureteral catheter in the treatment of persons with pyelonephritis and other renal conditions. Ordinarily, in lavage of the renal pelvis, the ureteral catheter is withdrawn immediately.

The inlying catheter, first recommended for the relief of obstructive aneuria and nontuberculous renal infections, now is used: (1) for the relief of aneuria of the obstructive type, (2) in the treatment of patients with acute and chronic pyelonephritis, (3) for relief from pain resulting from ureteral obstruction, (4) in cases of ureteral injury following pelvic operations, and (5) as a method of drainage of the kidney after the repair of a vesicovaginal fistula.

Eisendrath employs small roentgen-ray ureteral catheters, as the coating is more durable on the opaque than it is on the nonopaque catheter. Only a single catheter is inserted into the ureter of the affected side. Irrigation of the renal pelvis is not necessary, as there is ample drainage through the lumen or alongside the inlying catheter. The time the catheters can be left in place varies. If they tend to be expelled, a small urethral catheter can be introduced into the bladder to avoid accumulation of urine.

Crosbie, in discussing Eisendrath's paper, states that he believes drainage should be reserved for cases of obstruction, in which the pelvis of the kidney cannot drain itself. A ureteral catheter cannot be left in long without causing a certain amount of injury to the ureter.

Merritt states that he had found the failure to irrigate the renal pelvis to be the cause of catheter blockage in many cases, and for this reason he now uses two catheters irrigating with sterile water and then a solution of mercurochrome-220 soluble through one.

Livermore maintains that stasis is the chief cause of infections of the kidney. Although there may be a definite focus of infection, it does not lodge in the kidney unless stasis is present or the dosage overwhelming. If there is obstruction, the kidney will unquestionably be infected.

Bumpus states that another type of case which has not been mentioned in the treatment with the inlying catheter is pyelitis of pregnancy.

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23. Eisendrath, D. N.: Inlying Ureteral Catheter in Treatment of Pyelonephritis and Other Renal Conditions, *J. A. M. A.* 89:2170 (Dec. 24, 1927).

duced experimentally in the living dog by the administration of ether. A further possible source of this fat is suggested by the present study.

The presence of fat embolism following death from causes other than trauma has been remarked by several observers. Scriba<sup>2</sup> found fat embolism present in 52 per cent of all bodies. In addition, many specific diseases have been found to be associated with fat embolism. To put these on record in juxtaposition to our present results, we quote the following paragraph from our previous report:<sup>1</sup>

Carrara<sup>3</sup> reports fat embolism present at necropsy in 22 per cent of deaths from cardiovascular-renal disease and in 44 per cent of burns. Catsaras<sup>4</sup> found fat emboli in the lungs in eighteen of sixty-seven cases of postinfluenzal pneumonia. Gröndahl<sup>5</sup> reports fat embolism in two cases of eclampsia, four cases of diabetes, and two cases of phosphorus poisoning; Winkler<sup>6</sup> in two cases of acidosis, and Winogradow<sup>7</sup> as occurring regularly in potassium chlorate poisoning. In addition to these repeated findings there have been authentic reports of fat embolism having occurred, without history of trauma, in one or more cases of each of the following conditions: carbon monoxide poisoning,<sup>8</sup> profound sepsis,<sup>8</sup> chronic alcoholism,<sup>8</sup> chloroform narcosis,<sup>8</sup> diabetic retinitis,<sup>8</sup> phlegmonous gastritis,<sup>8</sup> acute pancreatitis,<sup>8</sup> chronic tuberculosis,<sup>8</sup> menstrual suppression, hepatitis, splenitis, carcinomatosis and sarcomatosis.<sup>8</sup> (The last five conditions are cited from the literature by Warthin.)

On account of the generally accepted observation that if fat embolism occurs, it will be seen in the lung (because of the slower blood current and unsupported capillary walls), our observations were limited to lung tissue. This limitation gave us also a simpler standard for comparison. We have examined the available lung tissue in fifty unselected cases that were subjected to autopsy by the department of pathology of Washington University. These cases were not numerically consecutive, but they were consecutive with the necessary proviso that lung tissue had been preserved and filed. They were known to us by serial number until the tissue had been sectioned, stained and diagnosed for fat embolism. Sudan III was uniformly used for staining. After our diagnoses were recorded, we referred to the files of the pathologic department for postmortem diagnoses. We thereby prevented any preconceived ideas from influencing the result.

It is to be noted that the material available consisted of only one piece of tissue in most cases. In those instances in which disease of the lung was present, the specimen usually included the diseased portion of the

2. Scriba: *Deutsche Ztschr. f. Chir.* 12:118, 1879.

3. Carrara: *Freidreich's Bl. f. gerichtl. Med.*, 1898, vol. 49.

4. Catsaras, J.: *Presse méd.* 26:618 (Sept. 4) 1920.

5. Gröndahl: *Deutsche Ztschr. f. Chir.* 111:56, 1911.

6. Winkler: *Ztschr. f. orthop. Chir.* 45:616, 1924.

7. Winogradow: *Virchows Arch. f. path. Anat.* 190:92, 1907.

8. Bantin, C. F.: *Diabetic Lipemia Retinalis and Fat Embolism*, J. A. M. A. 86:546 (Feb. 20) 1926.

9. Warthin: *Internat. Clin.* 4:171, 1913.

## FAT EMBOLISM

### II. INCIDENCE AT POSTMORTEM \*

EDWIN P. LEHMAN, M.D.

UNIVERSITY, VA.

AND

ROBERT F. McNATTIN, M.D.

ST. LOUIS

In an earlier report on uncompleted studies on fat embolism,<sup>1</sup> the conclusion was reached that fat embolism is not necessarily traumatic in origin. This conclusion was based partly on experimental work and partly on published reports of the occurrence of fat embolism in non-traumatic cases. At that time, our personal experience did not include any instances of the latter type in the human being. Further, we found that search for fat emboli is not a routine in pathologic examination post-mortem. It therefore seemed desirable to check earlier authors by a search through unselected postmortem material for cases of fat embolism.

In our previous observations, the question was also raised as to the problematic rôle of fat embolism in the production of symptoms and death even in extremely severe cases. We found that dogs would tolerate without symptoms an amount of free fat in the blood stream considerably greater, weight for weight, than the amount that could be freed in the human being by the ordinary fracture, even of the femur. Our conclusions on this figure are somewhat modified by later injection experiments now being prepared for publication; nevertheless, we shall report a discrepancy in tolerance that still casts doubt on certain post-mortem diagnoses of fat embolism as a cause of death. It was hoped that the present series of examinations of material observed at autopsy would yield information concerning the quantity, distribution and character of fat emboli in various disease states that might throw some light on this second question.

In our earlier studies, we concluded that the fat found as embolism in nontraumatic cases probably appeared by the coalescence of the ultra-microscopic particles of fat normally occurring in the blood plasma. This coalescence was attributed to a breaking down of the physiologic emulsion from physical or chemical changes in the blood and was pro-

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\*From the Department of Surgery of Washington University and the Barnes Hospital.

1. Lehman, E. P., and Moore, R. M.: Fat Embolism: Including Experimental Production Without Trauma. *Arch. Surg.* 14:21 (March) 1927

TABLE 1.—*Degree of Embolism in Fifty Unselected Cases*

NO FAT EMBOLISM		Age	Operation	Trauma
No Fat				
2901	Prematurity .....	Premature	0	0
2909	Acute purulent mastoiditis; hemorrhage into brain .....	10 wks.	0	0
2918	Asthma, bronchial; bronchitis, acute and chronic .....	60	0	0
2945	Congenital atresia, common hepatic duct.....	6 wks.	0	0
2952	Enterocolitis, acute; bronchopneumonia.....	4½ mos.	0	0
2968	Tumor of cerebellum.....	29	7 mos. ago 24 hrs. ago	0
2984	Congenital heart disease.....	6 mos.	0	0
2986	Coronary thrombosis; rupture of heart.....	59	0	0
3006	General purulent peritonitis following perforation of gastric ulcer .....	49	5 days ago	0
3008	Carcinoma of head of pancreas, metastasis to liver .....	55	0	0
3315	Miliary tuberculosis (general) 3 weeks, post-partum .....	25	0	3 wks. (labor)
Leukocytic Fat Only				
2949	Acute bacterial endocarditis, four transfusions .....	28	0	0
Fat in Alveolar Exudate Only				
2947	Pulmonary tuberculosis; tuberculous pneumonia .....	24	0	0
FAT EMBOLISM				
Slight				
2905	Lobar pneumonia; chronic tuberculosis.....	52	0	0
2910	Acute lymphatic leukemia.....	2	0	0
2916	Excision of cecum; acute suppurative peritonitis .....	6	Recent	0
2922	Endocarditis, chronic and acute; pulmonary thrombosis .....	44	0	0
2925	Glioma of brain.....	30	Recent	0
2931	Glioma of brain; hemorrhage, postoperative....	5	Recent	0
2936	Cholecystitis and cholelithiasis; general peritonitis; abscesses of liver.....	50	6 days ago	0
2938	Acute purulent otitis media and mastoiditis, bilateral .....	2 mos.	0	0
2941	Endocarditis, chronic .....	39	0	0
2946	Acute lobar pneumonia.....	45	0	0
2950	Carcinoma of stomach, with metastases.....	43	0	0
2951	Hypertrophy and dilatation of heart; endocarditis, chronic .....	40	0	0
2955	Abscess of lung; pyemia.....	?	0	0
2958	Adenoma of thyroid; auricular thrombus.....	59	0	0
2962	Polycystic kidney, bilateral.....	42	Recent	0
2964	Cellulitis of thigh, with abscess; bronchopneumonia .....	46	2 days ago	0
2965	Aneurysm of arch of aorta (wiring operation) .....	51	1 year ago	0
2989	Lobar pneumonia; empyema, thoracic.....	33	0	0
2994	Status lymphaticus; old operative scar for nephrostomy .....	1½	Old	0
3010	Chronic myelogenous leukemia; bronchopneumonia .....	26	0	0
3011	Toxemia of pregnancy; incision, peritonsillar abscess .....	36	Recent	0
3020	Syphilis, congenital .....	4 mos.	0	0
Moderate				
2883	Carcinoma of cervix; acute pelvic peritonitis...	42	0	0
2895	Carcinoma of kidney; pyonephrosis.....	52	0	0
2914	Toxemia of pregnancy; retained placenta.....	21	0	Recent (labor)
2930	Abscess, subdiaphragmatic; cholecystectomy....	50	Recent	0
2957	Mastoiditis, acute, bilateral; paracentesis tympani .....	15 days	Recent (see col. 2)	0
2961	Fracture, ribs, multiple; emphysema, subcutaneous .....	86	0	Recent
2975	Arterial sclerosis, involving coronary artery....	58	0	0
2996	Hypertrophy of prostate; pyelonephritis; pericarditis, adhesive .....	40	0	0
3005	Chronic ulcerative colitis with polyposis; acute purulent peritonitis; ileostomy.....	54	Recent	0
3017	Aneurysm of abdominal aorta with rupture; syphilis .....	62	0	0
Marked				
2933	Subperiosteal abscess, femur; suppurative arthritis, hip; pyemia.....	7	0	0
2935	Adenocarcinoma, colon, with metastases; spontaneous fistula .....	57	8 days ago	0
2930	Arthritis, knee, suppurative; thrombosis of coronary artery; incision and drainage, knee joint .....	63	Day of death	0
Embolism in Single Area of Section				
2906	Lymphatic leukemia .....	52	0	0
2923	Glioma of pons; bronchopneumonia.....	35	Recent	0

organ. It is possible that this fact influenced the results; however, as intracapillary fat was sought, the presence of disease, such as pneumonia or tuberculosis, should tend rather to diminish the fat found through inflammatory occlusion of capillaries. If fat was found in the vessels of a small segment of one lung in nondiseased areas, the conclusion that it occurred elsewhere in the lungs is highly probable.

Intracapillary globules of fat, except as discussed later in relation to fat found in the phagocytes, were diagnosed as fat embolism. Most of these were large enough actually to plug capillaries. The number of these was estimated, and the degree of embolism classified as shown in table 1. "Slight" fat embolism (table 1) was diagnosed when considerable search through a section was necessary before fat was found. "Moderate" fat embolism (table 1) signifies that the fat was easily found, but not in the majority of microscopic fields. "Marked" fat embolism (table 1) means that fat was found in the majority of fields. In two cases, the embolism found was limited to one area of the section. These two cases were given a separate classification (table 1) on the chance that this distribution might invalidate the diagnosis. For the reasons to follow, however, it is permissible to assume other areas elsewhere in one or both lungs.

As we have observed in our experiments on injection of fat <sup>10</sup> and in these present specimens, even marked grades of embolism are patchy in distribution. This is shown by areas of intense distribution of fat next to areas free from fat. For this reason, the demonstration of a few definite fat emboli (as listed in table 1) must be considered positive instances of fat embolism.

We did not find fat tissue in the peribronchial zone in the human material studied as we did in the dog. This may be because a block of tissue in the former does not reach the major bronchial ramifications as a block of the same size does in the latter.

Phagocytes containing fat were rather less regularly observed in the human being than in the dog. This probably can be ascribed to the fact that death in the human being is frequently preceded by starvation as it is not in the experimental animal. We were careful, however, to assure ourselves that no fat diagnosed as emboli was in the bodies of phagocytes. Occasionally, we found collections of fat-containing leukocytes and in the same zone much intracapillary fat (fig. 1). In one instance, this was entirely in the form of minute droplets of the same size as those in the cells. This was reported as showing only leukocytic fat (table 1). In other instances, in addition to such small droplets, globules larger by several diameters than any found in the cells were present. These droplets were reported as emboli. It seems possible that a source of free fat in the blood stream may be the destruction of fat-containing leukocytes as well as the breaking down of the physiologic emboli of



The results of this study confirm earlier conclusions that fat embolism is an extremely common postmortem observation in all kinds of conditions, traumatic and nontraumatic. If the proportion found in this series of fifty cases should hold true through a larger experience, more than

TABLE 2.—*Proportionate Division of Fat Embolism in Fifty Unselected Lungs*

			Per Cent
No embolism.....		13	26
Embolism.....		37	74
Slight.....	22	44%	
Moderate.....	10	20%	
Marked.....	3	6%	
Single area.....	2	4%	
Total.....		50	

TABLE 3.—*Relationship of Trauma to Occurrence of Fat Embolism in Fifty Unselected Lungs*

	No Fat Embolism	Per Cent
Traumatic.....	3	23
Nontraumatic.....	10	77
	13	
	Fat Embolism	
Slight		
Traumatic.....	9	41
Nontraumatic.....	13	59
Moderate		
Traumatic.....	5	50
Nontraumatic.....	5	50
Marked		
Traumatic.....	2	66.6
Nontraumatic.....	1	33.3
Single areas		
Traumatic.....	1	50
Nontraumatic.....	1	50
	Summary	
Traumatic.....	17	40
Nontraumatic.....	20	54
	37	

TABLE 4.—*Occurrence of Fat Embolism in Traumatic and Nontraumatic Cases in Fifty Unselected Lungs*

		Per Cent
Traumatic cases.....	20	
No embolism.....	3	15
Embolism.....	17	85
Nontraumatic cases.....	30	
No embolism.....	10	33.3
Embolism.....	20	66.6

half of all fat embolism is not associated with trauma. The variety of diagnoses in nontraumatic cases in which we have found fat embolism is great. Certainly no one influence can be detected. Although, in our tables, the assumption is made that trauma is the determining cause of fat embolism in those cases in which it occurs in the history, the frequent

the plasma in nontraumatic cases. This is borne out by the fact that, with the one exception noted, whenever leukocytes were filled with fat, embolism also occurred.

The statistical analysis of the results of this study is reported in tables 2, 3 and 4. Of course, in such a small series, no emphasis can be put on the actual percentage estimations as indicating definite rates of incidence. They serve, however, to make certain conclusions tenable. The striking facts obtained from this analysis are as follows: 1. Definite fat embolism occurs in more than half of all lungs examined at

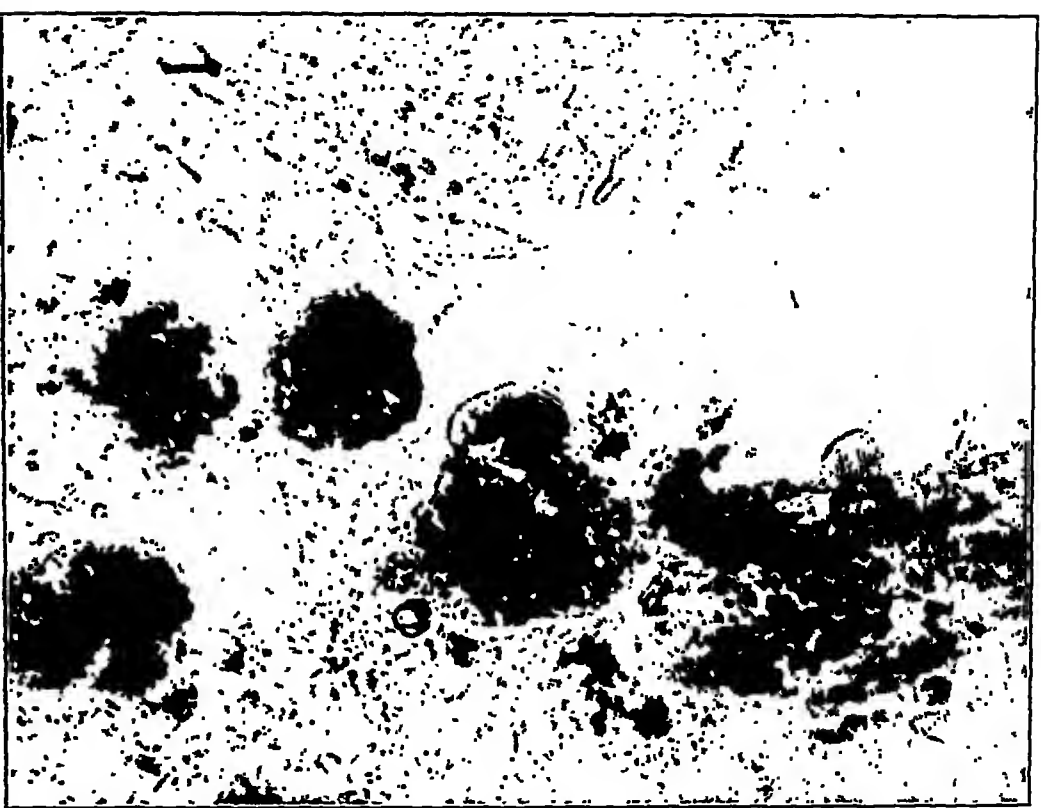


Fig. 1.—Fat emboli and fat-filled phagocytes; showing the difference in size between globules of free fat diagnosed as emboli and the much more minute particles in the cells (autopsy no. 2935);  $\times 986$ .

autopsy (table 2). 2. About one half of the lungs in which fat embolism occurs are from patients in whom there has been no history of trauma (table 3). 3. In a small proportion of cases in which definite trauma is recorded, no emboli could be found in a single examination of one lung (table 3). 4. Fat embolism is found in an overwhelming proportion of lungs from patients subjected to injury or operation (table 4). 5. Fat embolism occurs in more than half of the miscellaneous fatal diseases without history of trauma (table 4).



Fig. 4.—Fat emboli in a case of toxemia of pregnancy with retained placenta (autopsy no. 2914) ;  $\times$  986.

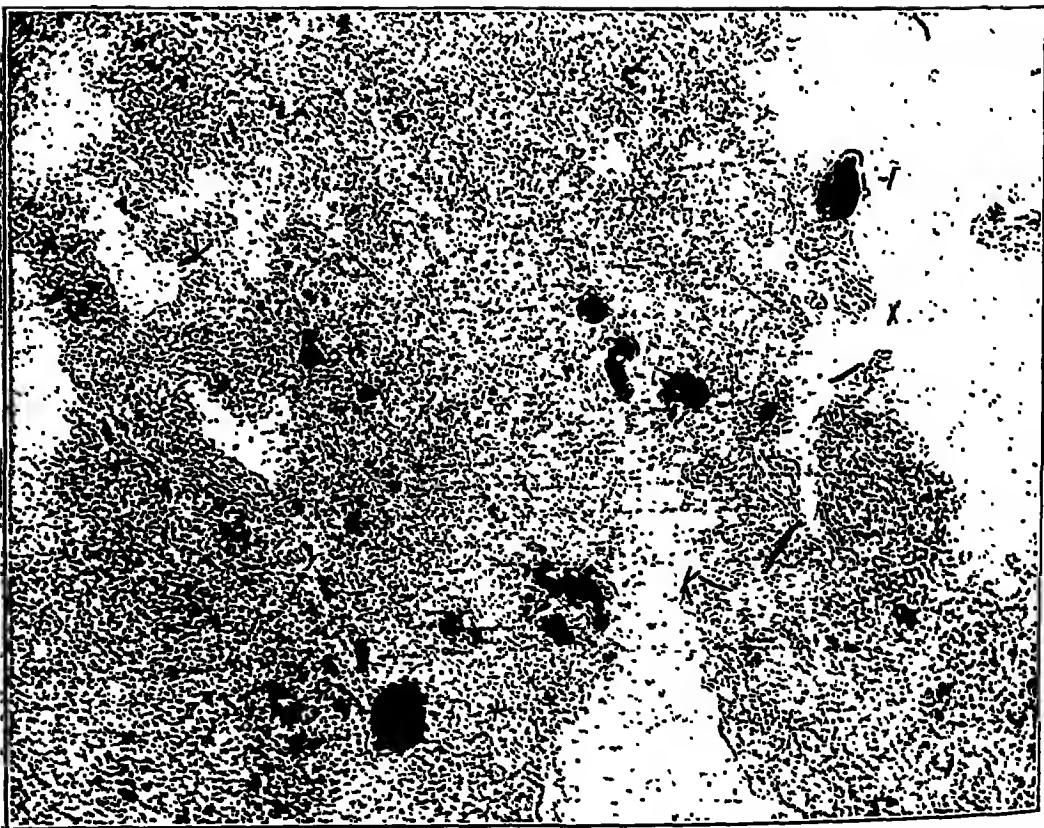


Fig. 5.—Fat emboli in case of suppurative arthritis of hip with subperiosteal abscess of femur in which operation was not performed (autopsy no. 2933). Low power magnification was used to show large number of emboli.

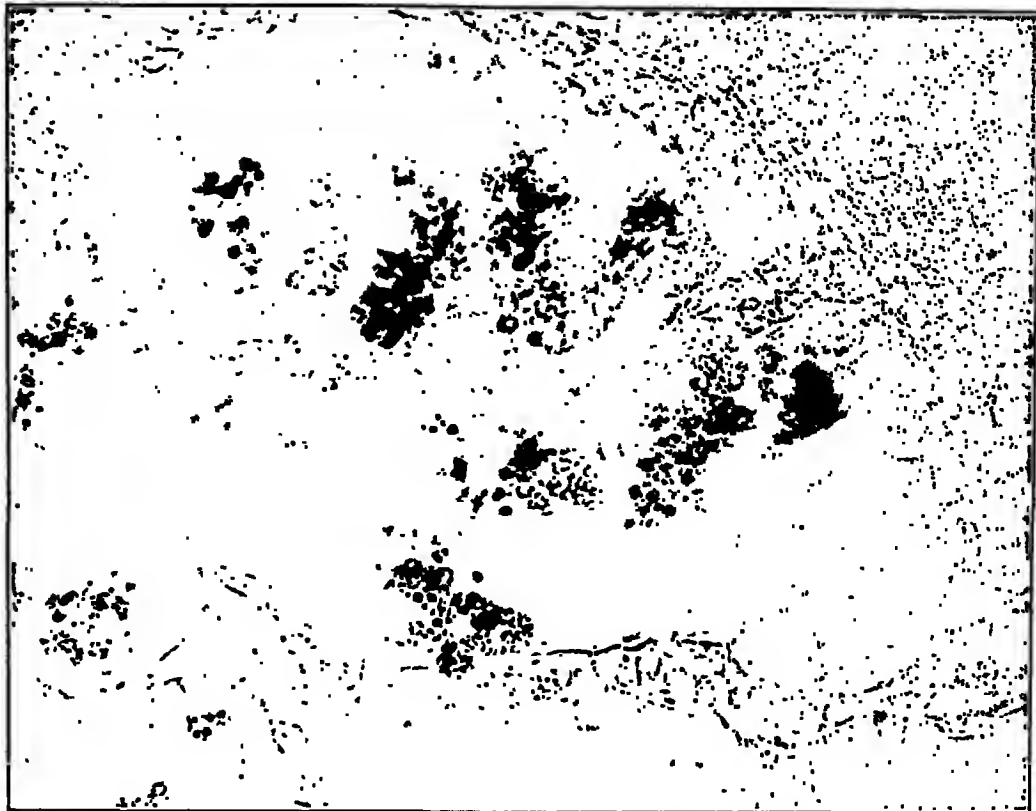


Fig. 2.—From a case of tuberculous pneumonia; showing free fat and fat-filled cells in the alveolar exudate and no fat in the alveolar walls (autopsy no. 2947). This illustrates a possible fallacy in Warthin's sign;  $\times 490$ .

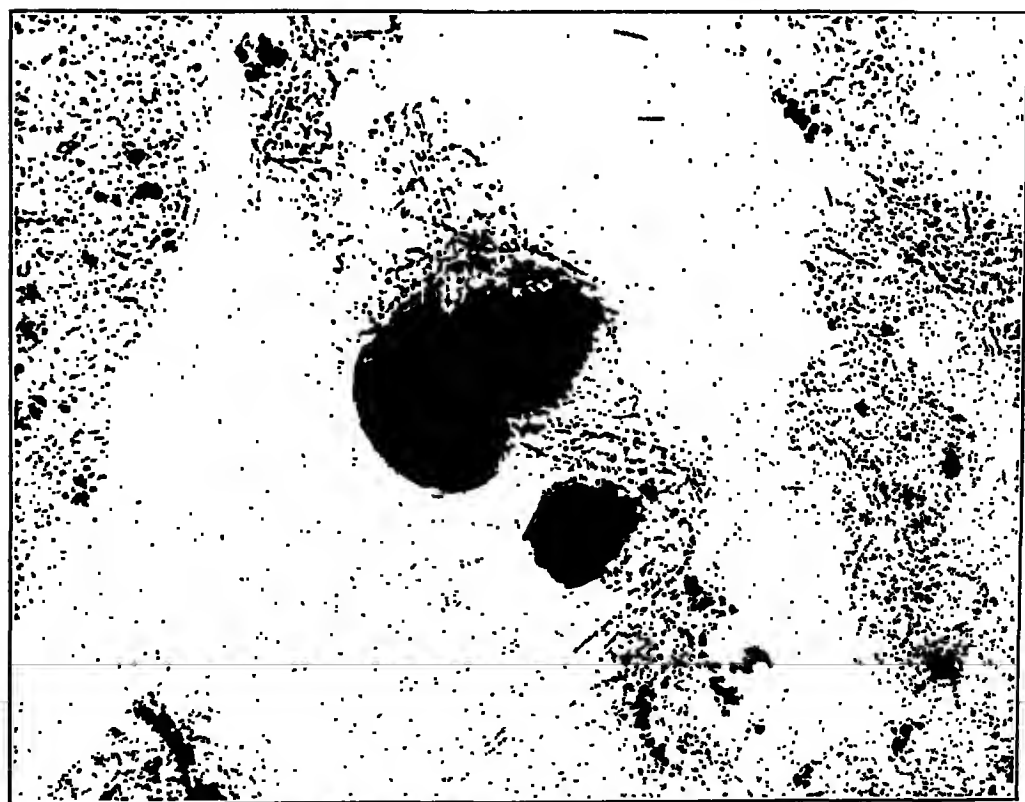


Fig. 3.—Fat emboli following multiple fractures of the rib (autopsy no. 2961). Here a globule of fat appears to be partially extruded into the adjacent alveolus, illustrating the mechanism of the appearance of fat in the sputum (Warthin's sign of fat embolism);  $\times 490$ .

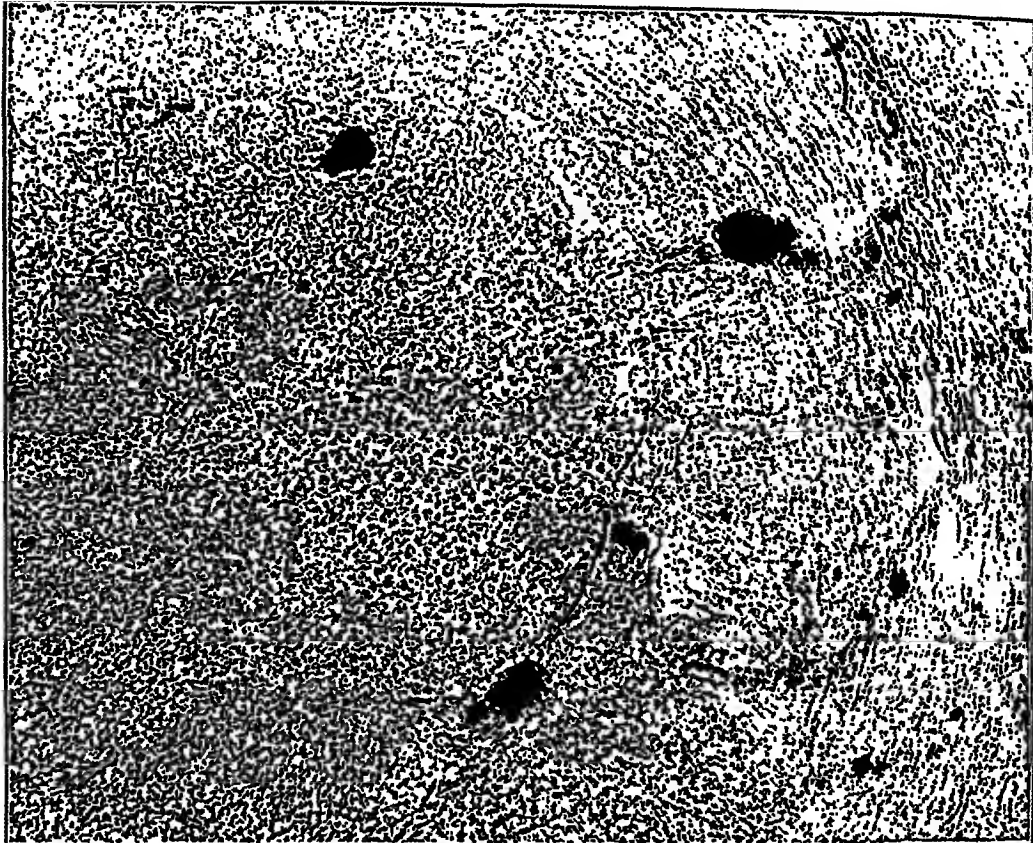


Fig. 7.—Slight degree of fat embolism (autopsy no. 2905). Postmortem diagnosis was lobar pneumonia and chronic tuberculosis. Three emboli were found in a single field;  $\times 183$ .

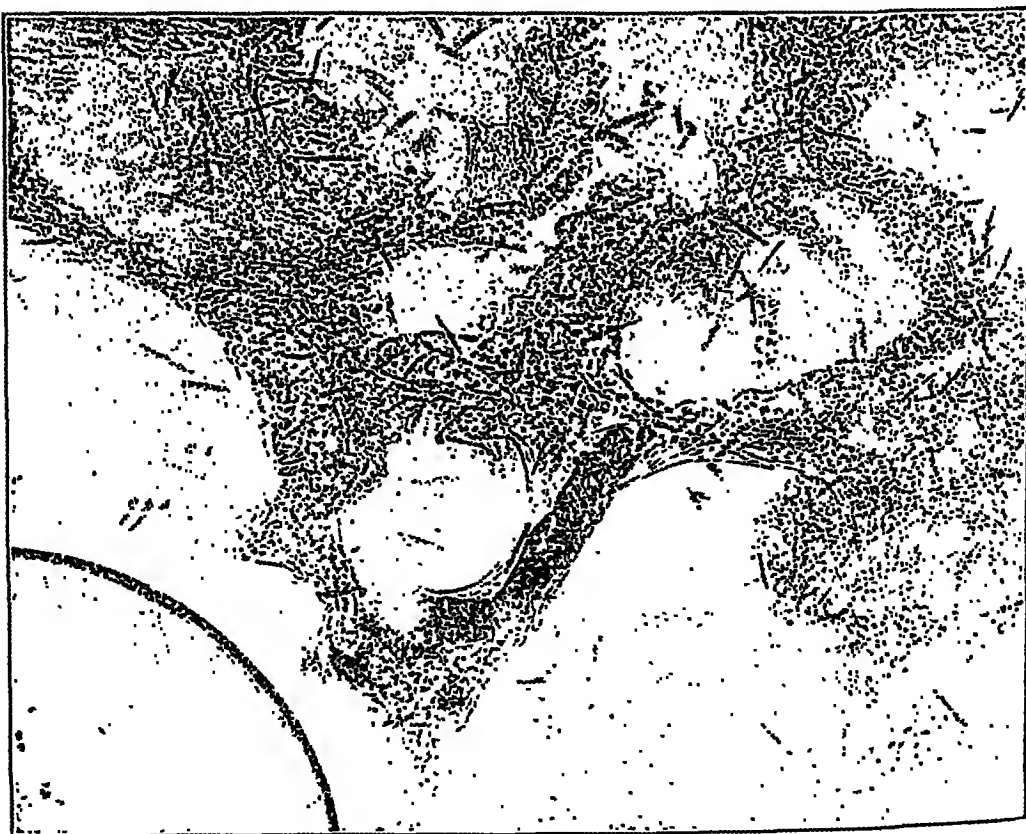


Fig. 8.—Several fat emboli in a case of carcinoma of the kidney and pyonephrosis (autopsy no. 2895);  $\times 198$ . Precipitated crystals of Sudan III are seen in this and other photomicrographs.

occurrence of fat embolism in nontraumatic fatal disease makes such an assumption not necessarily true. In other words, in some of the cases reported as due to trauma, other factors may conceivably have been the true cause.

What these factors are is a pressing problem. As reported earlier, there is certain experimental evidence that they may consist in physical and chemical changes in the blood, converting the physiologic emulsion of the plasma into free fat. This has been accomplished in the dog by the administration of ether. In studies of artificial emulsions in the test tube,



Fig. 6.—Fat emboli in case of suppurative arthritis of knee with coronary thrombosis. This patient was subjected to incision and drainage of the knee joint on the day of death (autopsy no. 2960);  $\times$  490.

there is suggestive evidence that the products of protein decomposition may possibly be blamed. Further studies along these lines have so far not been successful in confirming this suggestion.

When one considers these facts together with the experiments already referred to, one is forced to the conclusion that the presence of fat embolism in the lung after trauma does not justify the conclusion that such fat has been caused by the trauma or that it has caused death. Unquestionably there are cases of multiple fractures showing immediate symptoms, early death and blood at postmortem loaded with fat,



# ARTERIOVENOUS ANEURYSM OF THE BRAIN\*

WALTER E. DANDY, M.D.

BALTIMORE

The intracranial arteriovenous aneurysms here described are not peculiar to the brain. With the exception of differences of detail due to environment, they are essentially the same as arteriovenous aneurysms situated elsewhere in the vascular system.

The discovery of an arteriovenous aneurysm is always credited to William Hunter.<sup>1</sup> Enthusiastic phlebotomists of that period prepared two perfect examples of arteriovenous aneurysm for Hunter, which he was quick to recognize. His description of the signs and symptoms left little to be added, even at the present time. At the point of the communication between the artery and the vein, he recognized a loud hissing murmur and a strong tremulous thrill; large tortuous venous sacs were seen to pulsate; the brachial artery was greatly enlarged and serpentine cephalad to the arteriovenous fistula, but distal to it, the artery became smaller than on the other side. He was able to reduce the size of the veins, stop their pulsation and eliminate both the murmur and the thrill by pressing on a localized spot, which he recognized to be the opening between the artery and the vein. It was Hunter who first suggested the term "anastomosis" to denote the union of the two vessels.

To arteriovenous aneurysms of traumatic origin have since been added a great group with precisely the same clinical features, but in which the characteristic vascular changes have been present since birth. Virchow<sup>2</sup> referred to cases of Krause (Wm.) and Breschet as demonstrating beyond doubt the congenital origin of such cases. He also mentioned a case which Langier watched during the patient's life and in which he performed dissection after the patient's death; a free communication was found between the posterior auricular artery and a nearby vein. There are now many cases in which dissections of these aneurysms at operation or necropsy have demonstrated communication between a large artery and a contiguous vein by one or more aberrant vessels which could have arisen only as errors of vascular development in the embryo. In recent years, remarkable examples of these anomalous congenital communications in the neck and extremities, as disclosed at operation, have been reported by Halsted,<sup>3</sup> Rienhoff<sup>4</sup> and Reid.<sup>5</sup>

\* From The Johns Hopkins Hospital and University.

1. Hunter, W., cited by Callender: Bull. Johns Hopkins Rep. 19:260, 1920.

2. Virchow: Die Krankhaften Geschwülste, Berlin, 1863, vol. 3.

3. Halsted, W. S.: Congenital Arteriovenous and Lymphaticovenous Fistulae, Tr. Am. Surg. Ass., 1919.

4. Rienhoff, Jr., W. F.: Congenital Arteriovenous Fistula, Bull. Johns Hopkins Hosp. 35:271, 1924.

5. Reid, M. R.: The Effect of Arteriovenous Fistula upon the Heart and Bloodvessels, Bull. Johns Hopkins Hosp. 31:43, 1920.

in which so far as we know at present, it must be considered that the patients died of fat embolism. On the other hand, in any case of trauma with delayed symptoms, no matter how rich the blood in free fat, one must question the direct relationship of the trauma to the fat embolism and the relationship of the fat embolism to the symptoms. It is at least conceivable that the influences causing symptoms and death are also the influences causing freeing of fat in the blood stream.

There is one interesting note to be added. In a case of tuberculous pneumonia observed at autopsy (table 1, no. 2947), a large amount of fat was found in the alveolar exudate and none in the blood vessels (fig. 2). It is, of course, common to observe fat in the alveoli when fat embolism is present (fig. 3). On this basis, Warthin's sign of fat embolism was devised, namely the presence of fat in the sputum. The present observation demonstrates that fat can occur in the air spaces of the lung without embolism; in other words, Warthin's sign may not be as clearcut as is generally thought.



and eliminating not only capillaries but even the great venous and arterial trunks of the early embryo. It is evident that the retention of the original vascular connections between arteries and veins will readily explain the origin of the adult arteriovenous aneurysms. Dr. Halsted had in mind the arteriovenous aneurysm with aberrant congenital connecting channels. But it would seem that the maldevelopment of the original vascular bed would similarly explain the nests of abnormal vessels which are interposed between the arteries and veins and which replace the normal capillary bed.

Arteriovenous fistulas of traumatic origin are practically impossible in the brain, because the principal arteries and veins are not in juxtaposition as are the vessels of the head, neck and extremities. Arteriovenous aneurysms between the internal carotid artery and the cavernous sinus are exceedingly common, but as they are really outside the cranial chambers, and as they are in point of origin rather laws unto themselves, they need not be considered here. They are dependent on an anatomic arrangement which is not duplicated anywhere in the body. As the internal carotid arteries traverse the cavernous sinus in their passage through the base of the skull, a traumatic rupture of one of the arteries by a fracture of the base of the skull must inevitably result in an arteriovenous fistula, unless or until the arterial opening is repaired. The nomenclature of lesions which should really be included under arteriovenous aneurysms is most confusing. Being so dependent on the personal equation for the interpretation, they are reported under many titles, i.e., *angioma cavernosum*, *varix aneurysmaticus*, *angioma arteriale racemosum*, *angioma plexiforme*, *aneurysma cirsoidea*, *aneurysma serpentina*, *aneurysma anastomotica*, arteriovenous aneurysm, *tumor cirsoideus*, and particularly by the Germans as *Rankenangiom*—a term first applied by Virchow. Rienhoff<sup>4</sup> suggested a simple and sensible revision of the nomenclature of all vascular dilatation and communications into (1) venous, (2) arterial and (3) arteriovenous aneurysms, thereby discarding the term *hemangioma* at least for major lesions. This classification meets my full approval. In the group of arteriovenous aneurysms, the various terms “cavernous,” “racemose,” “cirroid” and “serpentine,” whether applied to arteries or veins, are merely descriptive of a superficial expression of a lesion and not of the fundamental pathologic process. A long as the term *hemangioma* is employed when an arteriovenous connection exists, there must always be uncertainty as to whether the tumor is arterial or venous. As a matter of fact, they may be either or both, but regardless of these superficial differences there is a direct communication through the vascular abnormality which has replaced the normal capillary bed. Moreover, the outward expression of an arteriovenous aneurysm, i.e., the arterial tortuosity and dilatation and the

Finally, there is a third group of cases in which an arteriovenous communication is established through the medium of a mass of abnormal vessels which take the place of the usual capillary bed, erroneously known as angiomas because of the impression that they are new growths; the true character of these lesions has long been obscured. The component vessels may be atypically arterial or venous, or both may be combined. Virchow discussed these tumors at length, and with some hesitation classified them under the heading "*angioma racemosum arteriale*." The following excerpt from his "*Krankhaften Geschwülste*" shows his grasp of the real underlying pathologic process:

Finally there remains that form of angioma, in which the vascular enlargement is outspoken and in which the character of the tumor is more in the background. Many of these forms are not to be understood in the light of oncology. They are often classified with *angiomata* and one cannot make a true line of demarcation between them and *angiomata*. Their difference lies principally in the fact that the process is diffuse, and that dilatation of both arteries and veins is present. These tumors have recently been called by John Bell *aneurysma per anastomosin*, and by Walker perhaps better, *aneurysma anastomoseon*.

Another group of vascular tumors so well known, even at the present time, as *angioma cavernosum*, were included by Bell under his *aneurysms per anastomosin*. Virchow referred to Dupuytren's experiments to prove that in these tumors injections of colored substance passed freely from the artery into the veins through the intermediary tumor. Virchow, though not conceding the arteriovenous communication, noted the fact that in some cases of cavernous angiomas (venous tumors) the artery is dilated and tortuous just as in true arteriovenous aneurysms.

It was Virchow's view that these arteriovenous aneurysms (or angiomas) were not new growths in the usual sense, but were of congenital derivation. Subsequent embryologic and pathologic researches demonstrated that no other explanation is tenable.

Professor Halsted,<sup>3</sup> whose interest in this subject extended over a period of several years, and who stimulated the splendid researches and publications of Callender,<sup>6</sup> Reid,<sup>5</sup> Holman<sup>7</sup> and Rienhoff,<sup>4</sup> approached the origin of arteriovenous aneurysms from the vascular anlage in the early embryo. It is known that the adult system of arteries and veins is derived from a general capillary network; that both arteries and veins form from this capillary network; that the final arterial and venous systems are derived by extensive evolution of a vastly different primitive system. This metamorphosis is accomplished by shifting, consolidating

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6. Callender, C. L.: Study of Arteriovenous Fistula with an Analysis of Four Hundred and Forty-Seven Cases, *Johns Hopkins Hosp. Rep.* 19:260, 1920.

7. Holman, E. F.: Physiology of an Arteriovenous Fistula, *Arch. Surg.* 7:64 (July) 1923.

been included, though the status of both is doubtful because the description of the venous outlets is inadequate. Several cases heretofore classified as cases of angioma, and usually assumed to be similar to those collected here, have been excluded. Among them are the cases of Oppenheim,<sup>17</sup> Sweasey-Powers,<sup>18</sup> Lewandowsky and Selberg,<sup>19</sup> Cassirer and Mühsam,<sup>20</sup> Uyematsu,<sup>21</sup> Creite, Abrikosoff,<sup>22</sup> Lechner,<sup>23</sup> Versé,<sup>24</sup> Rossolimo<sup>25</sup> and Bruns. It has also not been possible to include the cases of Isenschmid,<sup>26</sup> because neither observations made at operation nor those made at autopsy establish the clinical diagnosis. In one of his cases at least, the diagnosis is almost surely correct for, in addition to a well defined extracranial arteriovenous aneurysm, Jacksonian epileptic attacks were of long standing. The symptoms that I have considered essential for the diagnosis of an arteriovenous aneurysm have been, first and foremost, marked fulness and enlargement of the veins of exit; second, an increased size and tortuosity of the artery entering the snarled mass of vessels. Without the enlarged veins on the cortex or elsewhere one cannot assume the existence of an arteriovenous fistula.

The seeming infrequency of this lesion cannot be judged by the small number of cases assembled from the literature. Were this true, the lesion would be rare indeed. The eight cases which occurred at the Johns Hopkins Hospital among about 600 cases of verified tumors of the brain during a period of five years, are perhaps a better index of its relative frequency. In clinics on which neurologic material is concentrated, arteriovenous aneurysms apparently occur in from about 0.5 to 1 per

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17. Oppenheim, H.: Die Geschwülste und die syphilitischen Erkrankungen des Gehirns, in Nothnagel's Practice, vol. 9, p. 20.

18. Sweasey-Powers, W. J.: Ein Fall von Angioma cavernosum des Gehirns, *Ztschr. f. ges. Neurol. u. Psychiat.* **16**:487, 1913.

19. Lewandowsky, M., and Selberg, F.: Ueber Jacksonsche Krämpfe mit tonischem Beginn und über ein kleines Angiocavernom des Gehirns, *Ztschr. f. d. ges. Neurol. & Psychiat.* **19**:336, 1913.

20. Cassirer and Mühsam: *Berl. klin. Wchnschr.* **17**:755, 1911.

21. Uyematsu, S.: A Case of Haemangioma Cavernosum of the Cerebrum, *J. Nerv. & Ment. Dis.* **52**:388, 1920.

22. Abrikosoff, A. S.: Ein Fall von Angiona arteriale racemosum der Arterial basilons und der beiden arterial communicans posterior, *Zentralbl. f. allg. Pathol.* **22**:210, 1911.

23. Lechner, Ellen: Ein Beitrag zur Kasuistik der Hirnangiome, *Beitr. z. klin. Chir.* **125**:174, 1922.

24. Versé: Demonstration eines in die Substanz des Kleinhirns eingebetteten Aneurysma serpentinum et sacciforme der Arteriae Cerebri posterior Sinistra, *München. med. Wchnschr.* **58**:544, 1911.

25. Rossolimo, G. S.: Zum Ausgang von Gehirnoperationen, *Deutsche Ztschr. f. Nervenhe.*, vol. 6; *Neurol. Zentralbl.* **15**:714, 1896.

26. Isenschmid, R.: Die klinische Symptome des cerebralen Rankenangioms, *München. med. Wchnschr.* **59**:243, 1912.

engorgement of the veins leaving the tumor, are doubtless identical whether the communicating channels are exclusively arterial or venous or predominantly one or the other.

In attempting to gather the cases of arteriovenous aneurysms of the brain, the records of venous aneurysms and the various subdivisions of angiomas have been reviewed, and most of them have been collected from these groups. For example, there is no more perfect example of an arteriovenous aneurysm than the one pictured in Krause's colored plate,<sup>8</sup> but which he calls a venous angioma. On the other hand, cases reported as Rankenangioma and cirroid aneurysma, and therefore presumably arteriovenous aneurysms, have been excluded from this group because the absence of changes in the arteries and veins leading to and from the tumor has suggested a pure venous lesion. Other cases reported as venous, which undoubtedly seem to be arteriovenous, are those of Astwazaturoff,<sup>9</sup> Steinheil,<sup>10</sup> Dürck, Kalischer,<sup>11</sup> Mühsam,<sup>12</sup> Eiselberg,<sup>13</sup> Campbell and Ballance<sup>14</sup> and others. Doubtless the teaching of Oppenheim and Krause was in large part responsible for the interpretation of these vascular lesions as venous.

#### FREQUENCY OF ARTERIOVENOUS ANEURYSMS OF THE BRAIN

The first arteriovenous aneurysm of the brain was reported by Steinheil<sup>10</sup> in 1895, or 138 years after William Hunter's<sup>1</sup> first reported arteriovenous aneurysms in the arm.

A total of twenty-two cases which seemed to represent this type of intracranial aneurysm have been collected from the available records. Two additional cases of Struppler<sup>15</sup> and Simmonds<sup>16</sup> (second case) have

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8. Krause, F.: *Chirurgie des Gehirns und Rückenmarks*, vol. 1, p. 88, 1908, English trans., New York, Rebman Company.

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and had complained of some stiffness in this arm. The attacks usually occurred in the early morning. He has had some trouble with his memory; he said that he often forgot most important things.

*Examination.*—A tenderness to deep pressure was revealed over the right parietal region. The patient said that there was a localized sore spot in this region (not over the tumor as later discovered). The neurologic examination did not reveal anything. The eyegrounds were normal. The roentgenogram of the head was negative. The Wassermann reaction of the blood was negative.

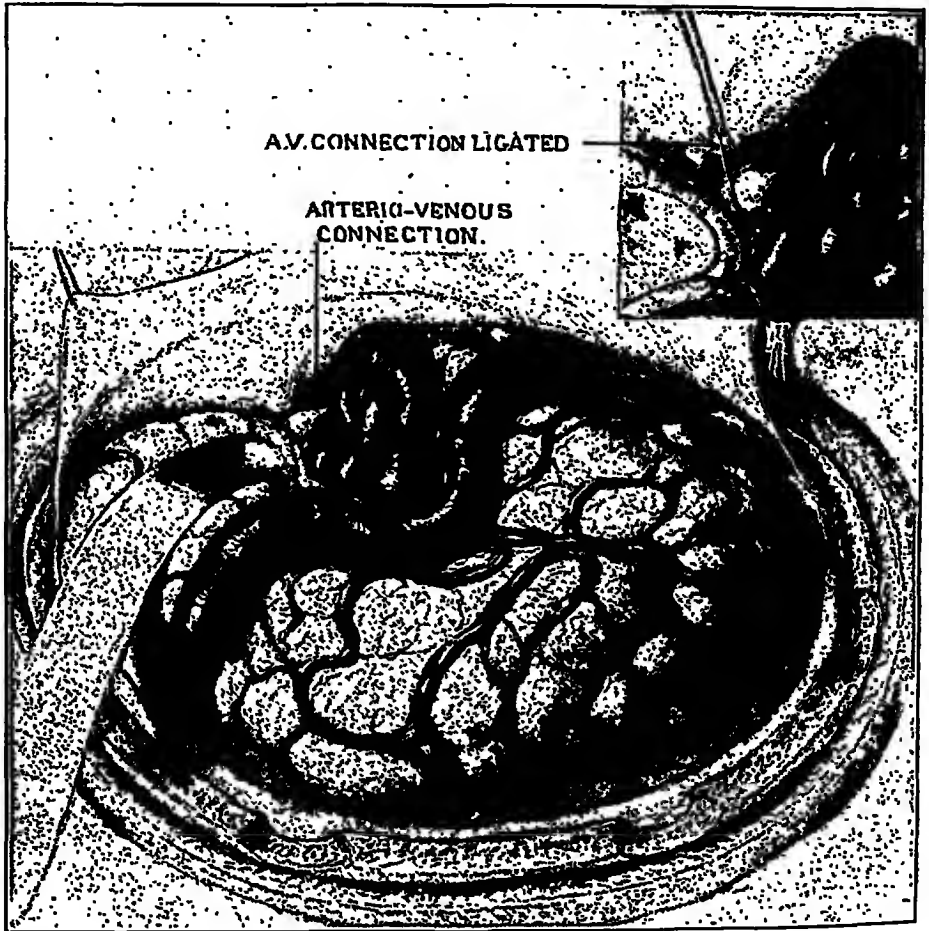


Fig. 2 (case 1).—An anomalous branch connecting the middle cerebral artery with the angiomatous mass. The transition from the artery to the vein is shown in the net work.

While he was in the hospital, an attack was observed by the nurse, but focal signs other than turning the head to the left were not seen. Urine was lost. Motor weakness did not follow the attack.

The injection of air into the cerebral ventricles showed dislocation of the ventricular system to the left side. The third ventricle was also bent obliquely to the left. The anterior horn of the right ventricle was smaller than the left. A diagnosis of right frontal tumor was made.

*Operation.*—Right craniotomy was performed. A group of tremendous engorged and tortuous veins covered the anterior half of the right temporal lobe, and to a much lesser extent the frontal lobe. They emptied into a huge sylvian

cent of the cases. It is clear that more cases will be disclosed at operation than at necropsy, because the symptoms (usually epilepsy) are not such as to require prolonged hospitalization. Most of the necropsies were obtained on patients who were brought to the hospital in coma resulting from cerebral hemorrhage. This number obviously represents but a small proportion of the afflicted persons.

#### CASES OF INTRACRANIAL ARTERIOVENOUS ANEURYSM

**CASE 1.—History.**—A well nourished, well built, muscular man, aged 52, an army officer, was suddenly and without warning seized with a severe clonic con-

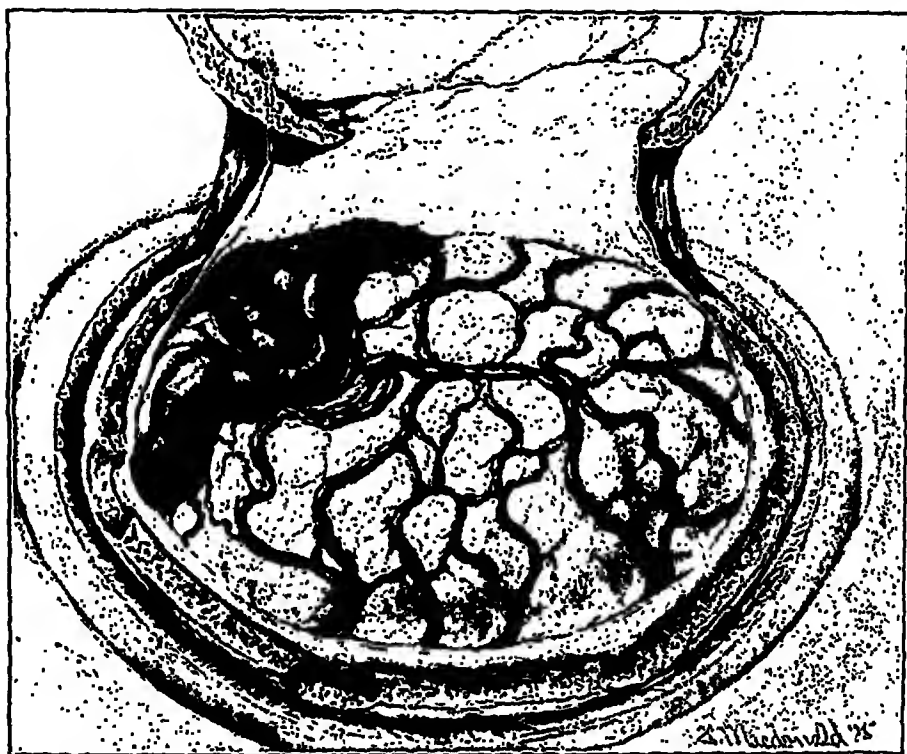


Fig. 1 (case 1).—Arteriovenous aneurysm showing a large sylvian vein emptying into the large anomalous vein crossing the temporal and frontal lobes. There is a distinct enlargement at the point of junction of these two veins; the rolandic vein is easily defined.

vulsion lasting about fifteen minutes. This attack occurred six years prior to examination, just after his return from France, where he actively participated in the World War. He had never had any kind of an attack before. For the next three years similar attacks occurred about once every two months; then for two years there was no attack, but for the past year they have appeared about every month. Recently, there have been petit mal attacks with loss of consciousness for from forty to sixty seconds, but no muscular contractions. One week ago he had a violent generalized headache; following this, a pain persisted in the right frontal region. His head turned to the left during the convulsions, but there was no other focal sign. At times he had had a dull aching pain in the fingers of the left hand



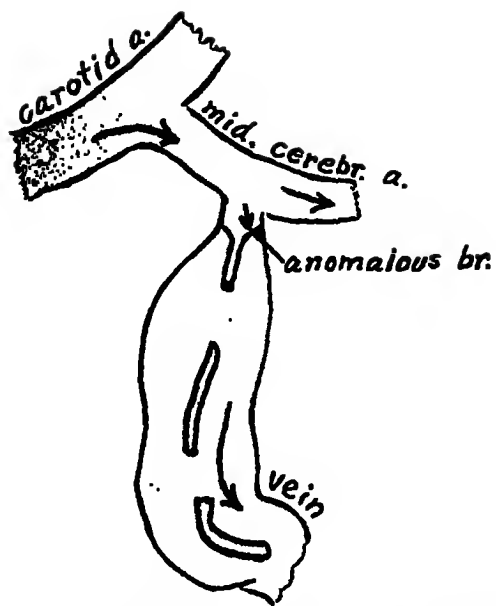


Fig. 3.—The direct communication between the artery and vein by means of an anomalous vessel.



was almost as large as the middle cerebral artery at this point. The arterial portion of the vessel was well isolated, surrounded by two silk sutures and ligated. The venous tumor immediately collapsed. We did not see any suggestion of a central tumor mass such as was present in other cases of the series from which the veins emerged. It was our impression that the condition was a pure arteriovenous fistula, produced by an anomalous vessel passing directly from the middle cerebral artery into a large venous trunk, which ultimately reached the sylvian vein. The great veins could be seen to connect with the sylvian vein.

*Postoperative Course.*—When the patient was coming out from under the effects of the ether, he complained of severe headache and weakness of the contralateral part of the arm and the leg. During the ensuing twenty-four hours, this side slowly became completely paralyzed, and his pulse rate steadily dropped to 60. Since the patient was somewhat drowsy, we suspected an extradural hemorrhage, but elevation of the bone flap did not show any collection of blood. The paralysis puzzled us, for our manipulations were entirely under the frontal lobe, too far afield from the motor tract to cause motor weakness, and seemingly remote from the middle cerebral artery. If the middle cerebral artery had by some chance been injured, why did the paralysis develop so gradually? We have also wondered whether the drop in the pulse rate might not be similar to the bradycardia noted by Holman as a constant sequel to the closure of arteriovenous fistulas in his series of dogs. Five days after the operation, recovery of function began in the left side and steadily progressed. Still unable to explain the cause of the hemiplegia, it is equally difficult to explain the recovery. Aside from a slight residual weakness of the left arm and hand and a slight limp, the patient was well three and a half years after the operation. Two and a half years after the operation, he had one convulsion; since then there have been no other seizures, either petit or grand mal, nor have there been any headaches or soreness corresponding to the old "localized tender spot." The spells of forgetfulness have disappeared.

*CASE 2.—History.*—A well nourished, normal looking boy, aged 19, sought relief from convulsions (1922). At the age of 15, he was seized with numbness in the left corner of his mouth. A "pricking sensation as of pins and needles" quickly followed and spread over the left side of the face. The tongue was pulled to the left, and it also had a similar "sensation as of pins and needles." The left side of the face twitched. The sensation spread to the left arm, but the arm did not twitch. The attack lasted only about one minute. The hand was weak for several minutes after the attack; consciousness was lost. Five months later, he was attacked by a convulsion while asleep. He foamed at the mouth, and urine was passed. During the following two months there were four more such attacks, all occurring during sleep, then a free interval of several months.

One year ago, a unilateral (left side) convulsion was not accompanied by loss of consciousness, and similar attacks have since occurred about once a month, always with the warning aura of numbness at the corner of the mouth. There has been only one unconscious spell during the past year; the hand and arm are always weak after such a spell.

*Examination.*—The results of the examination were negative. There was no objective evidence of motor weakness on the left side. The reflexes were normal and equal on the two sides. The roentgenogram was negative. The Wassermann reaction of the blood was negative. The preoperative diagnosis was probable cerebral tumor causing jacksonian epilepsy. A tumor was suspected because motor weakness followed in the wake of the convulsion.

*Operation.*—Feb. 11, 1922: Right craniotomy was performed. On the dural side of the bone flap, the inner table of the skull was eroded in a circular area

vein, joined at right angles a large anomalous vein which crossed the frontal lobe in a vertical direction and continued downward across the temporal lobe. There was no well defined rolandic vein. The network of veins dipped over the anterior margin of the temporal lobe, entirely obscuring the anterior pole. The largest venous trunk was over 1 cm. in diameter. The veins were a definite pink and were in striking contrast to the black veins elsewhere in the brain. One could easily see the blood rhythmically (with each heart beat) passing through the dilated thin walls of the veins. On palpation, a distinct thrill could be detected in the veins. Since any attempt to treat the aneurysm surgically appeared to involve a

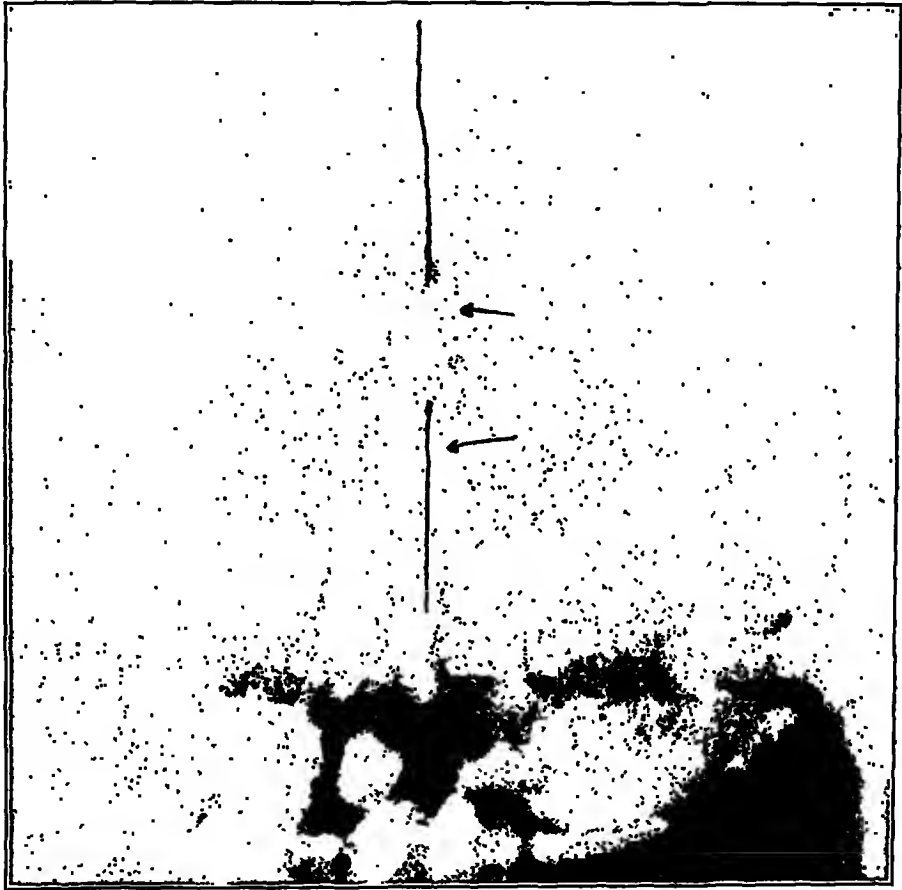


Fig. 4 (case 1).—Ventriculogram showing dislocation of the ventricles to the left and the deep third ventricle. The arrows indicate the dislocation of the ventricular system toward the left.

risk greater than my co-workers and I were justified in assuming, the dura was closed and the bone flap was replaced.

*Second Operation.*—Two weeks later the wound was reopened, the frontal lobe retracted and the inferior surface of the frontal lobe and the anterior pole of the temporal lobe well explored. Search was at once made for an arterial communication. A large anomalous branch passed from the middle cerebral artery (immediately distal to its origin) directly into the mass of engorged serpentine vessels. It was thick-walled and definitely arterial at its origin, but less than 0.5 cm. distally there was an abrupt transition to a thin-walled vein. This vessel

After consultation with the patient's brother, who realized the great danger involved, an attempt was made to extirpate the mass. It was hoped that the surface vessels might be ligated and the tumor undermined and included in a mass dissection of brain tissue, without actually coming in contact with the vessels of the tumor. As this was our first experience with this type of lesion, we little realized its extreme difficulties and dangers. The sylvian vein was tied with two silk ligatures and the vessel divided. We hoped to work through the cortex from this point mesially, but as there was not sufficient room, the line of attack was shifted to the mesial aspect of the tumor. The rolandic vein was doubly tied and divided. A remarkable resistance was encountered in ligating the vein. Usually a vein offers almost no resistance to the sliding knot, but in this instance the knot could be slipped down only step by step because of the pressure within the vein. Ligation and division of the rolandic vein were accomplished without incident. A few minutes later, however, while a subcortical dissection was being performed and preparation was being made to ligate additional vessels, a sudden burst of blood flooded the operative field. The rolandic vein had burst, not at the points of ligature but in the bulge of the vein about midway between the ligatures on its now isolated segment. The closure of the venous outlets had taken away too many of the channels of exit for blood from the tumor and the thin-walled rolandic vein, no longer able to withstand the added extra strain of increasing arterial pressure, burst at its weakest point. The bleeding became profuse. Pressure with cotton and gauze accomplished little more than to check the bleeding temporarily. A rapid extirpation of the mass was attempted, but the bleeding vessels multiplied. There was no cerebral tissue, only a skein of wormlike vessels which bled furiously. The carotid vein was tied in the neck, and while this reduced the bleeding so that tampons of cotton controlled it, shortly afterward the renewed pressure established by collateral again lifted the cotton pack, and the bleeding began anew. When it was again stopped, the patient's condition was so seriously affected that he died a few hours later.

**CASE 3.—History.**—A healthy looking man, aged 35, was referred by Dr. Ralph Greene, of Jacksonville, Fla., on Jan. 25, 1925, because of a general mental and physical breakdown, headache, double vision, periods of somnolence, slurring speech and staggering gait.

The patient's condition was said to have begun two years before examination with a staggering gait and a tendency to swerve to the left. He said that he would fall to the left any time when his eyes were shut. Diplopia had been present more or less continually for the past two years. Dizziness was frequent and disturbing. A thick slurring speech had been noticed for a month. Headaches had occurred irregularly, but were more noticeable when the patient was constipated. There was also pronounced mental impairment with paranoid trend. He was irritable and suspicious and adopted a superior attitude. His insight and judgment were poor. His speech was slurring and he quickly rambled over a number of subjects without cohesion and without meaning. He had formerly studied medicine and apparently did well until he stopped because of a dislike for the subject. His memory was uncertain. Convulsions, loss of consciousness, motor or sensory disturbances or difficulty in swallowing were not noted.

**Examination.**—The neurologic examination showed bilateral choked disk of 3 diopters in each eye. There were no obvious extra-ocular palsies to explain diplopia; coarse nystagmoid jerks of the eyeballs occurred when the patient looked far to the right or left. There was dysarthria; greatly diminished hearing in the left ear; slight ataxia in the heel to knee test, but not in the finger to nose



test; staggering gait; positive Romberg sign, the patient falling constantly to the left and no adiadokokinesis. He walked with a broad base.

There were bilateral positive Babinski and Oppenheim signs; otherwise the reflexes were normal. There were no motor or sensory changes. The Wassermann test of the blood was negative. A roentgenogram of the head was negative.

A tentative diagnosis of cerebellar tumor was made, but the pronounced mental changes were unexplainable.

Ventricular estimation showed both ventricles to be large and in free communication with each other (indigo-carmin test). The fluid was under greatly increased pressure.

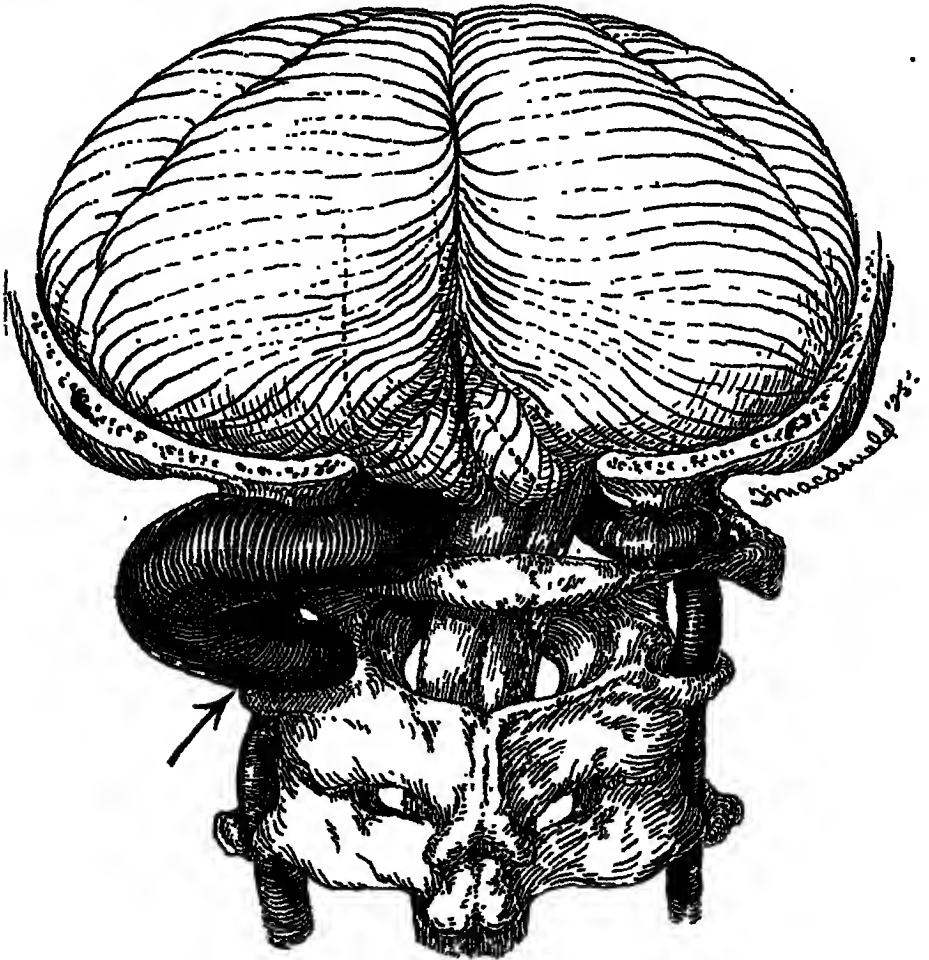


Fig. 8 (case 3).—Sketch of aneurysm showing the tremendous vertebral artery on this side. This diagrammatic sketch is intended to show the difference between the vertebral arteries on the two sides. The sketch is not accurate in that the bulge of the artery was between the atlas and the axis, but from the artist's view at the operation it might well have looked as it does. The artery was doubtless also enlarged below this point, though it could not be inspected at the operation.

*Operation.*—A cerebellar exploratory operation was performed. When the cerebellum was exposed, six large tortuous veins stood out in strong relief about equally on both cerebellar lobes. They converged to two large trunks at the border of the superior surface and dipped out of sight onto the tentorial surface

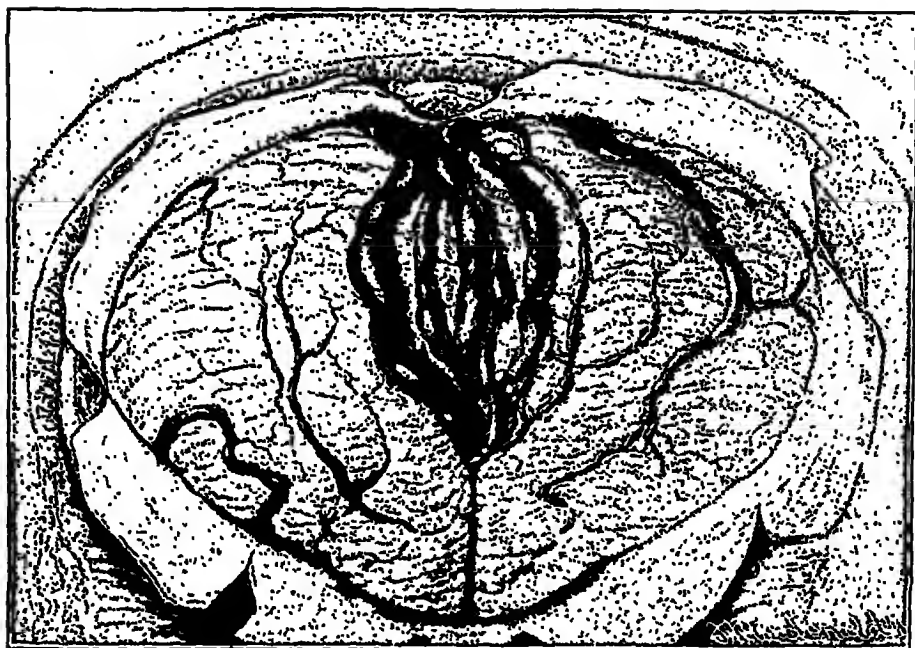


Fig. 6 (case 3).—Arteriovenous aneurysm in the posterior cranial fossa. The large veins on the surface of the cerebellum were lost under the dura.

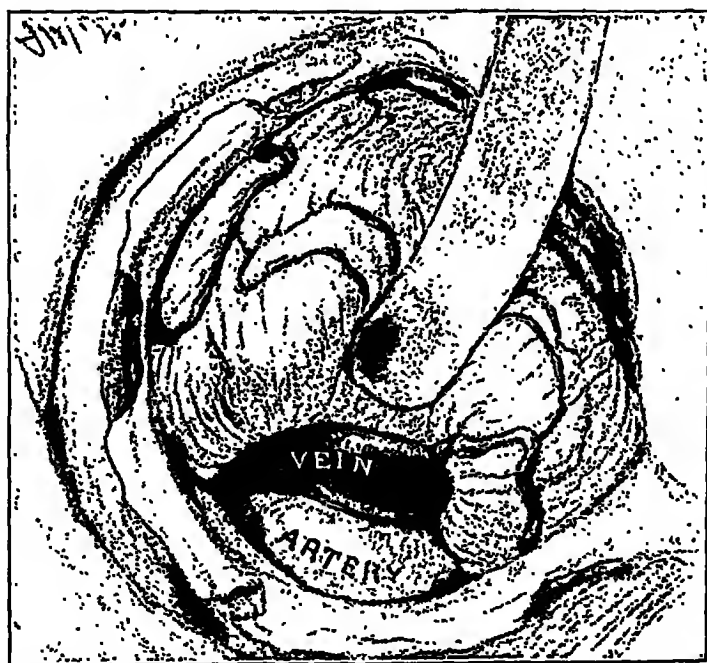


Fig. 7 (case 3).—Elevation of the left lobe of the cerebellum shows the big venous bed underlying and the tremendous vertebral artery beneath the vein.

wound was bulging and tight; immediately afterward it became soft and somewhat sunken, and remained so during the remainder of the patient's stay of a month in the hospital. A discharge note by Dr. Deryl Hart states that the bruit, formerly heard so strongly over both temples, could be heard only over the right (contralateral) temple. The gait was much improved; the Romberg, Babinski and Oppenheim signs were negative. Subjective diplopia still persisted.

Two and a half years later, the patient wrote that he had remained well and free from headaches, but, judging by his letter, there had not been any mental improvement.

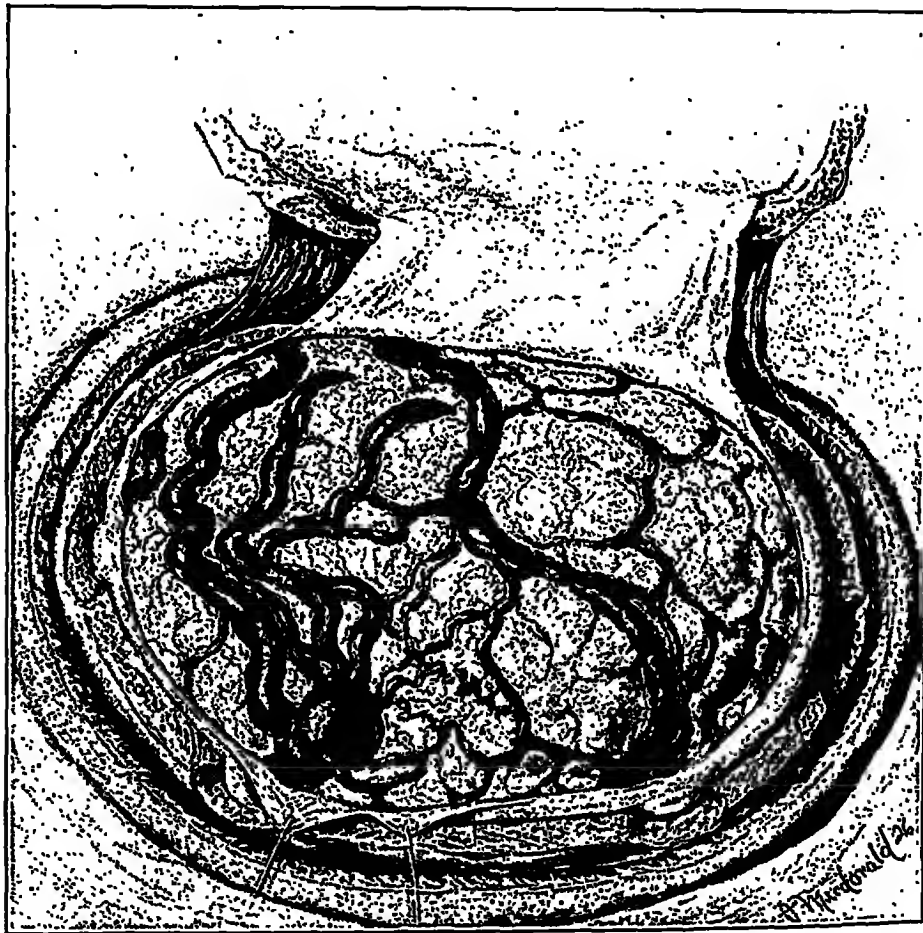


Fig. 10 (case 4).—A spider-like arrangement of veins abnormal in both size and position are directed toward the central swelling, which is just above and underlying beneath, and which can be palpated.

**CASE 4.—History.**—A sparely nourished man, aged 47, was referred by Dr. L. E. Stubbs and Dr. H. W. Curtis, of Newport News, Va., on Oct. 1, 1925, because of frequent jacksonian convulsions and some motor weakness. Six years before this, he was suddenly seized with a cramp in the left hand; this was immediately followed by weakness of the legs, loss of consciousness and a convulsion. He regained consciousness an hour and ten minutes later, but was so weak that he could not leave the bed for three days. A month later, he was seized with an attack similar in origin but less severe; consciousness was lost for only a few minutes. During the next three years, such attacks occurred with fair regularity





*Examination.*—The neurologic examination showed that there was some motor weakness of the left side of the face and of the left arm, but not of the leg. Sensation was not changed. Biceps and triceps reflexes were markedly increased on the left side. The knee jerks were slightly greater on the left; the Babinski sign was negative. The Wassermann reaction of the blood was negative.

A roentgenogram of the head showed a group of calcified areas in the right frontoparietal region. In the anteroposterior view, these extended almost from the surface to the midline. The shadows were linear and circular, and in one place there was a definite whorl. The shape of these shadows suggested a vascular pattern, and from the roentgen-ray observations alone, a vascular tumor was suspected.



Fig. 12 (case 4).—Patient after the cerebral exploration and after the ligation of the internal carotid artery on the affected side. The partial occlusion later became complete by the reaction around the rubber band which was used to restrict it.

*Operation.*—On Oct. 3, 1925, a left craniotomy was performed over the region so clearly defined in the roentgenograms. The inner table of the bone was much thinner. These changes of pressure were due to a localized dilatation along the course of a large tortuous cerebral vein in front of and below the face portion of the Rolandic area. From this venous center four large tortuous veins radiated as from the hub of a wheel (fig. 10). This venous dilatation was also situated almost in the center of an indurated subcortical mass, sharply defined by palpation and measuring about 5 by 5 cm. The large venous dilatation could be seen to pulsate, and when partially obliterated a thrill was imparted to the palpating finger. At each heart beat, the swirling red (arterial) blood could be seen through the walls of the vein. There seemed no hope of a successful

about every two months. Three years before coming to Dr. Stubbs and Dr. Curtis, he had the first attack in which he was conscious throughout. A cramp attacked the left hand, causing his hand to close into a fist; the arm quickly became rigid and drew up above the head. He had a sensation of being unable to catch his breath; he thought it grew dark about him, and it seemed as if his heart had stopped beating; profuse perspiration broke out. He thought he was going to die. He thought his left leg was paralyzed, for he could not move it; the muscles of his trunk did not seem to be affected. This attack lasted half an hour, gradually passing away. For the next two years, there were no

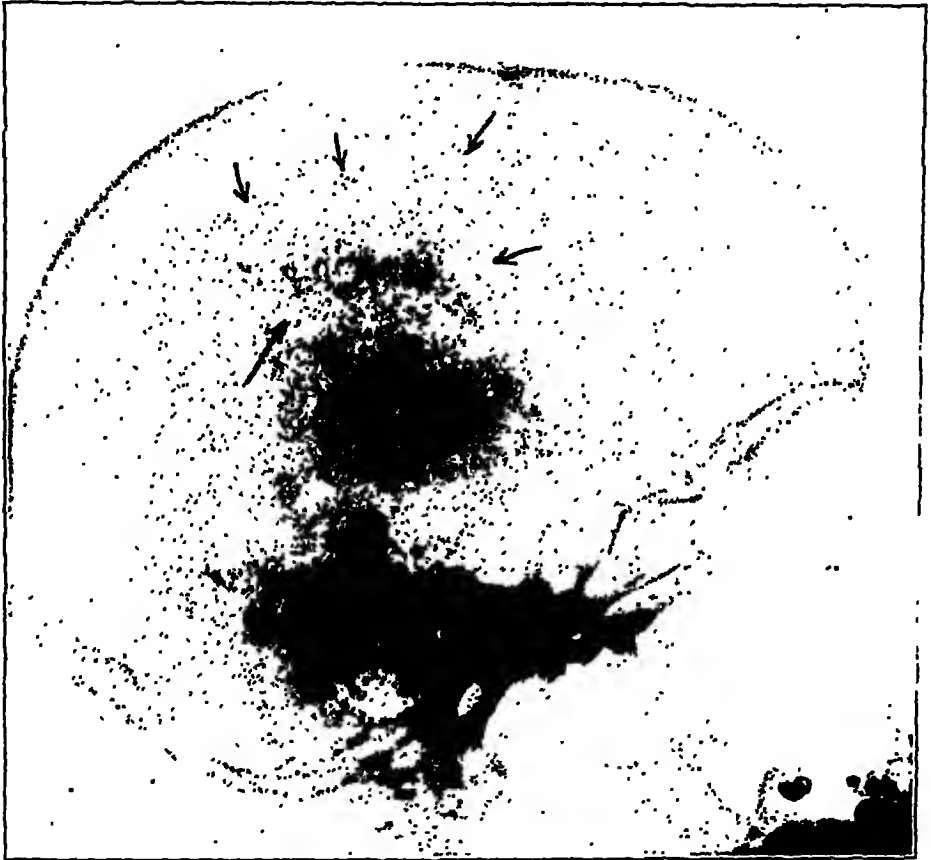


Fig. 11 (case 4).—Roentgen-ray observations. The arrows are directed toward the enormous shadows, and the whorl-like calcification of the vessel in the aneurysm is the most conspicuous shadow in the group.

more attacks (he was taking phenobarbital); then followed an attack like the last one. Since then similar attacks, without loss of consciousness, had occurred at intervals of about two months. After one attack the left arm and leg were paralyzed for half an hour, the function gradually returning. In addition, the left arm steadily became weaker, until it was considerably disabled. There had been only one attack at night, and no petit mal attacks. Severe headaches occurred after the attacks; with these exceptions, he did not have headaches. The attacks appeared to be induced by constipation, but not by exercise or excitement. Phenobarbital was definitely helpful; he ascribed the two years' free interval from attacks to this drug. There was no history of trauma.

A ventriculography showed that in the right postrolandic region there was a great defect which was in free communication with the body of the lateral ventricle. The loss of cerebral tissue was interpreted to be the sequel of the hemorrhage which had occurred seven months before. The actual tumor or aneurysm did not show, but was assumed to be alongside the cerebral defect.

*Operation.*—On July 21, 1925, a right craniotomy was performed. A plexus of large, tortuous veins obscured the brain just above the sylvian vein and below and posterior to the motor face area. The rolandic vein, which skirted the mass of superficial veins, was two or three times its normal size; the sylvian vein was also much enlarged. This circumscribed mass of veins dipped

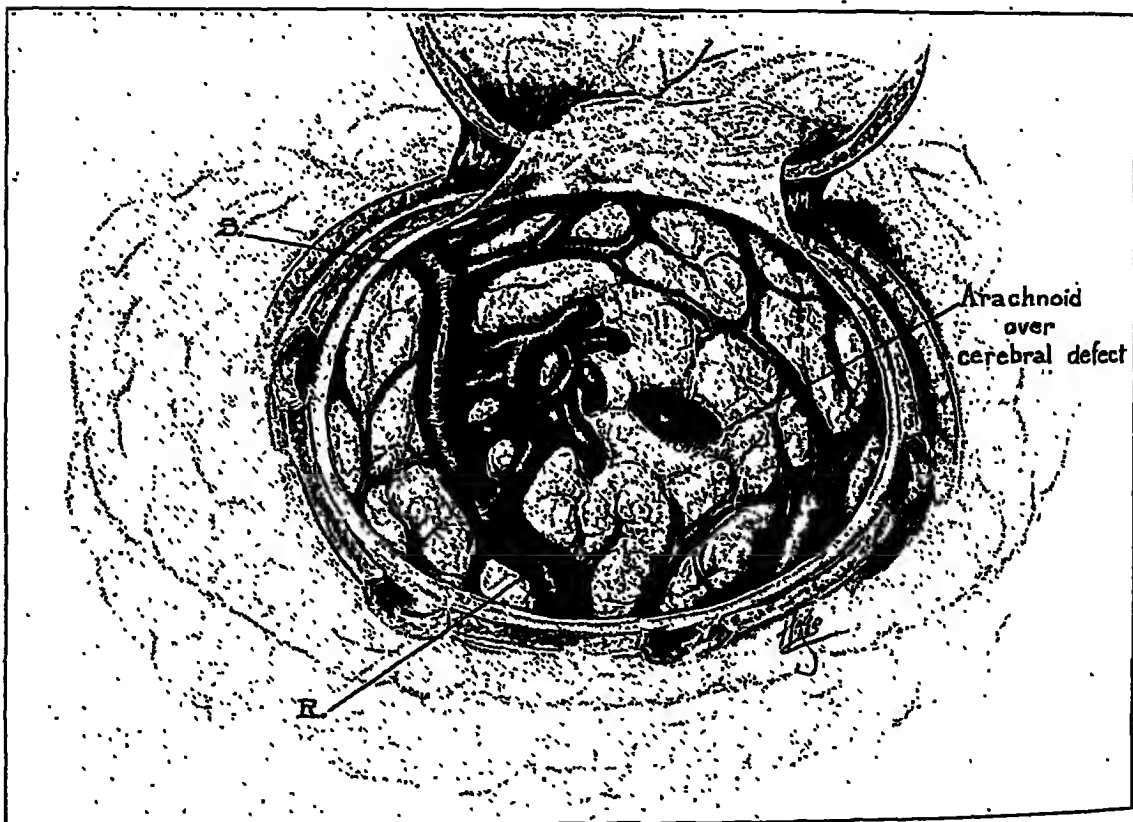


Fig. 13 (case 5).—The cluster of veins overlying and draining the mass of vessels below the surface of the vein. These veins abnormal in position empty into the tremendous rolandic vein which is continuous with an equally large sylvian vein. Arterial blood could clearly be seen in the veins. The cyst just posterior to the cluster of veins is the outer part of the defect which resulted from the cerebral hemorrhage which occurred several months previously.

into the cerebral cortex. Red arterial blood could be seen swirling in the rolandic vein with each heart beat. A thrill could not be felt.

About 1 cm. behind the venous plexus the meninges were transparent in an oval area about 1 by 1.5 cm. A cystlike dome was bulging upward from below. When this was opened, it proved to be the big ventricular dilatation (cerebral defect) indicated by the ventriculograms. The cerebral defect became larger below the surface and was nearly as large as a hen's egg. Its size was little reduced where it opened into the lateral ventricle.

surgical intervention for such a vicious arteriovenous lesion. A subtemporal decompression was made; it remained fairly full and tight after the operation.

*Second Operation.*—Three weeks later, it was decided to ligate the right common carotid artery. Because of the danger of this procedure at the patient's age, a partial occlusion was first made with a rubber band. Twelve days later, the wound was reopened, the artery was ligated above and below the band, and the intervening tissue (including the band) was excised. There was a rather extensive reaction of all the tissues contiguous to the rubber foreign body. The carotid artery was already completely occluded with firm fibrous tissue within its lumen. It was our impression at the time that this was a satisfactory method of inducing a gradual occlusion of the carotid. It would, however, be dangerous if eventual total occlusion of the internal carotid artery could not be tolerated. No untoward symptoms were noted at the time of partial ligation or subsequently when it became total.

When the carotid artery was exposed for ligation, a lumbar puncture was performed, and the height of spinal fluid was measured. On each temporary closure of the carotid artery (to test for possible symptoms of cerebral anemia), the spinal pressure became reduced from 280 to 255 mm. and returned to the previous normal level when the lumen of the carotid artery was again restored. The blood pressure rose from 168 to 175 each time the carotid artery was closed.

For five days after the operation, the decompression was markedly sunken, then becoming flush with the skin.

The convulsions disappeared for more than a year. They then returned in mild form, but after eighteen months had again become like the former attacks.

*CASE 5.—History.*—A well nourished man, aged 48, was first seen in coma in the medical service of the Johns Hopkins Hospital, on Jan. 21, 1925. During the past ten years, he had had four convulsive seizures with loss of consciousness and with involvement of the left arm and leg. He did not rouse from the attack he had just before his admission to the hospital. He had incontinence of urine and feces, a pulse rate of 44 and rapid, stertorous breathing. Gradually, the coma disappeared. A residual partial hemianesthesia, hemiplegia and homonymous hemianopsia were present on the left side when consciousness was restored. Eventually, all of these signs disappeared almost entirely. Bloody fluid was obtained from several lumbar punctures. He convalesced slowly, and when discharged from the hospital six weeks after the onset of coma, he was mentally confused and forgetful. There was no history of trauma.

Six months later (July, 1925), he had another attack, with unconsciousness, but it lasted only three or four minutes. Shortly afterward, he returned to the hospital for treatment. During the time since his comatose spell he had done some work, but had been morose and gloomy. After dinner he sat alone or went to bed, always shunning company. He was forgetful and at times confused.

*Examination.*—A slight homonymous defect was found in the left visual field; the left knee jerk was obtained only on reinforcement; the right, not at all. No motor or sensory disturbance remained on the left side. The blood pressure was 125 systolic and 85 diastolic. The Wassermann reaction of the blood was negative.

It was evident that the patient had had a cerebral hemorrhage in the parieto-occipital region. At his age, and with negative vascular signs, it was safe to assume the existence of an underlying tumor or aneurysm from which the hemorrhage had arisen.



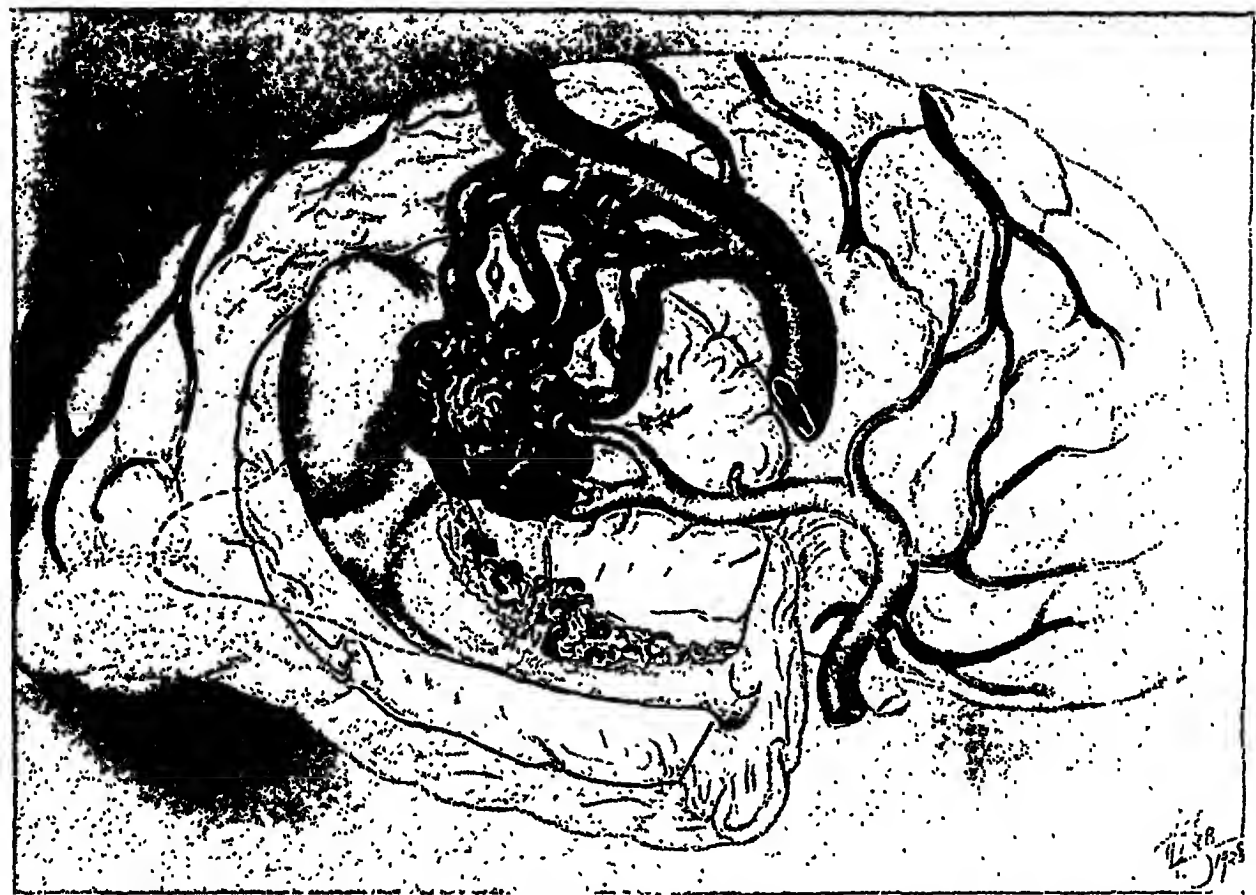
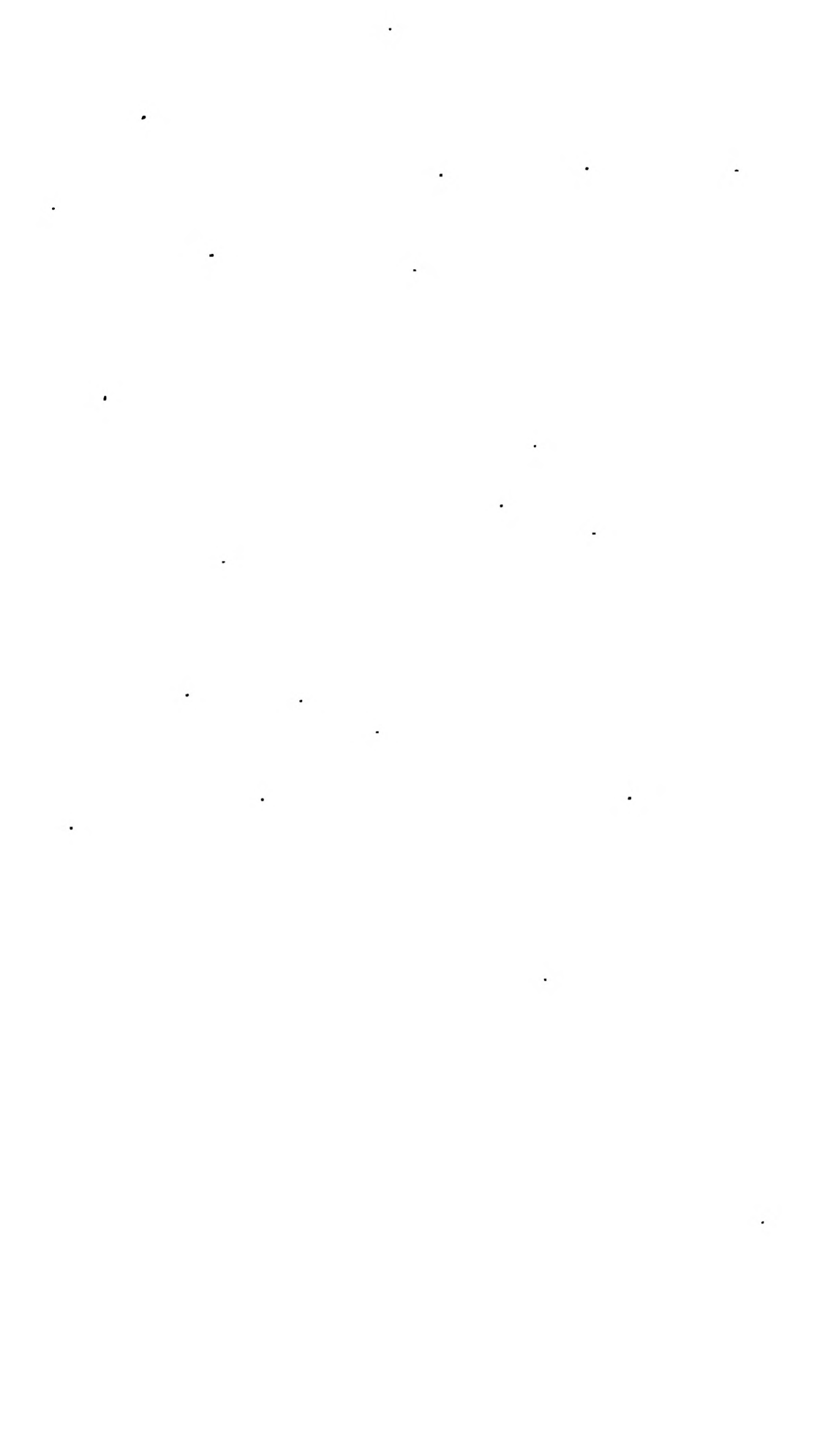


Fig. 14 (case 5).—Reconstruction of arteriovenous aneurysm from the necropsy specimen. The large middle cerebral artery terminates in the mass of vessels—the so-called angioma—whereas on the opposite side the middle meningeal artery continues on posteriorly. The vascular bed protrudes into the defect which has resulted from the cerebral hemorrhage and which communicates freely with the lateral ventricle.



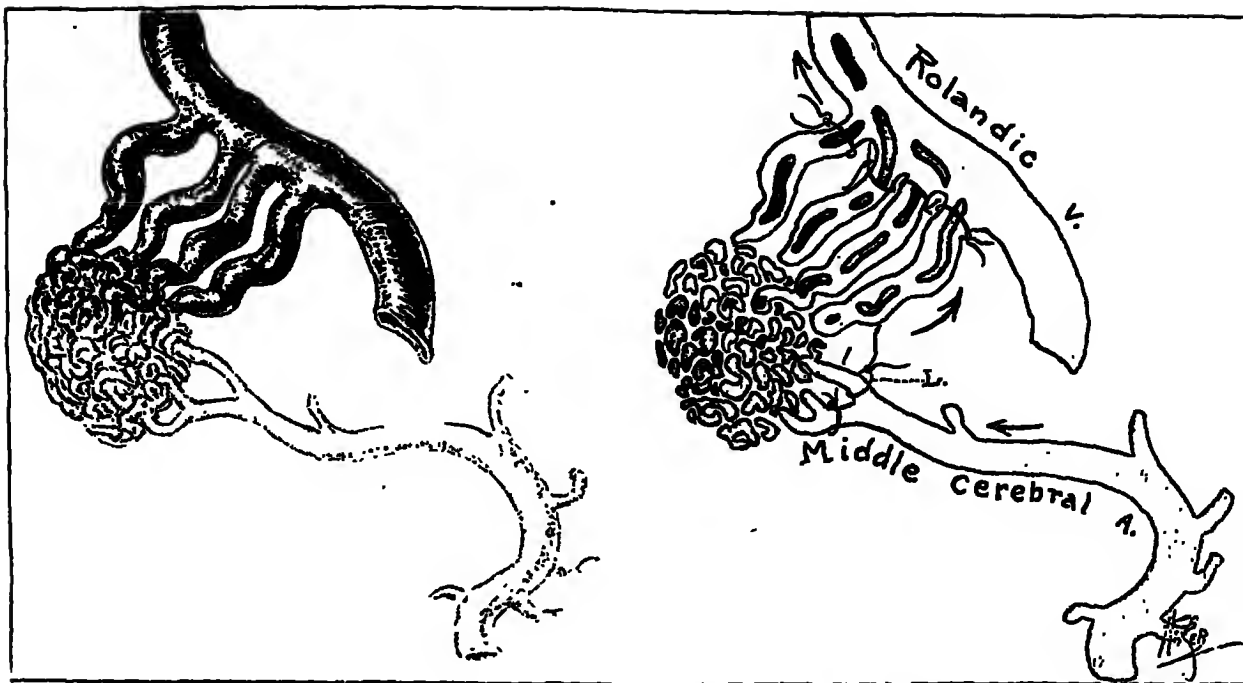


Fig. 15.—Diagram to show the construction and vascular arrangement of the arteriovenous aneurysm (case V, fig. 14). The vascular intracranial mass takes the place of the former capillary bed from which it doubtless is a congenital maldevelopment.

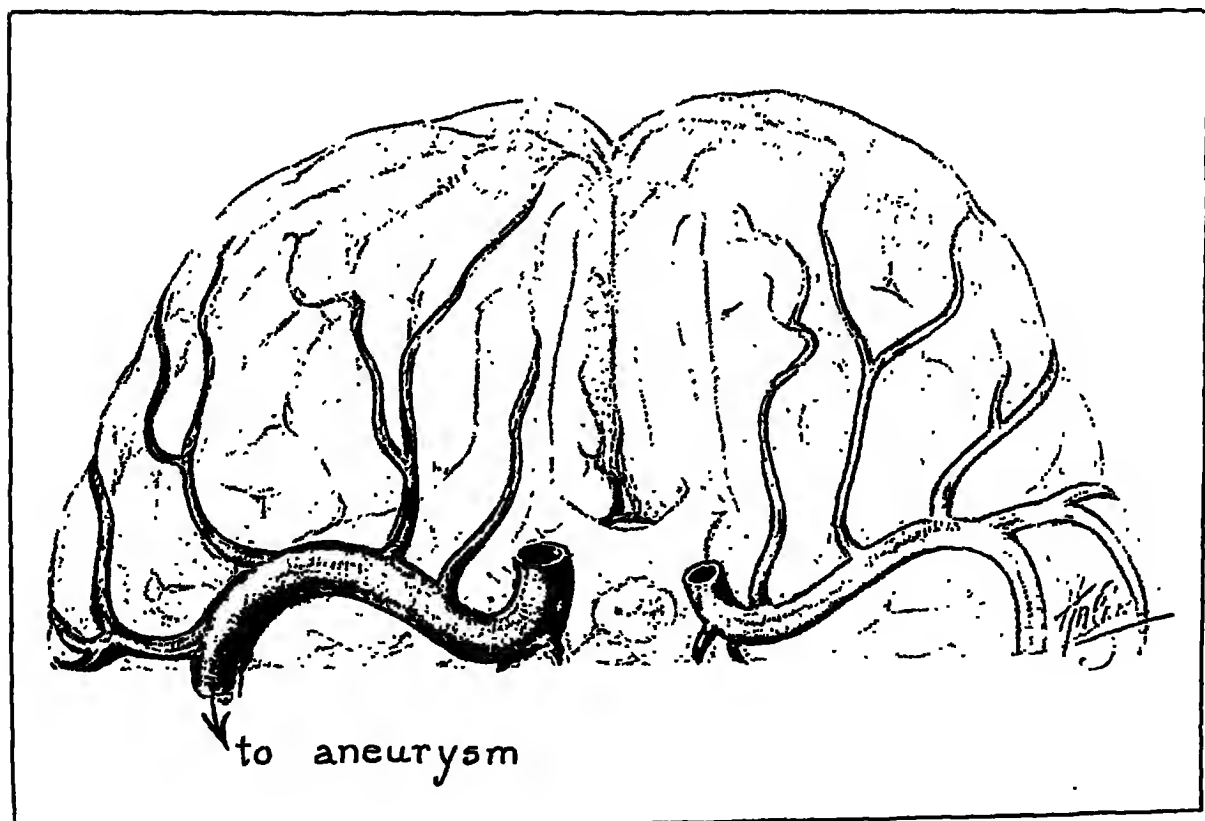


Fig. 16.—Sketch to show the relative size of the middle cerebral arteries on the normal and affected sides. The artery on the side of the aneurysm is considerably larger all the way to its origin in the carotid.



open ventricular system, this patient would surely have survived, for the hemorrhage would have been far less significant and easily handled. Our reasons for excising this tumor were: 1. The tumor was back of the rolandic area, and a hemiparesis could probably be avoided. 2. Owing to the protrusion of the arterial units into the cerebral defect, a cerebral hemorrhage would probably occur again and by flooding the ventricular system cause death.

The middle cerebral arteries of both sides were dissected after death. The right was from one-third to one-half larger, even to its origin at the carotid



Fig. 18 (case 5).—Ventriculogram of the affected side. The large shadow is the cerebral defect which has resulted from the old hemorrhage. It will be noted that the volume of air which filled the left ventricle was only enough to fill the defect in the right ventricle.

artery. The affected middle cerebral artery turned upward and terminated in the branches which entered the nest of vessels. The left artery, however, took an entirely different course in this region and for some distance continued backward toward the occipital lobe.

**CASE 6.—History.**—A well nourished young man, aged 31, complained of loss of vision, progressive weakness of the left arm and leg, headache and convulsions.

The first symptoms of onset, dating back fifteen years, were intermittent spells of blurred vision and headache across the forehead on the right side. These

In the anterior wall of the defect, several small, hard, dark gray nodules, from about 1 to 2 mm. in diameter, protruded into the cavity. Poorly covered by the white matter of the brain, they were recognized as vascular buds and as the outposts of a vascular tumor. Extirpation of the mass seemed possible and was attempted after ligation of the vessels on the surface of the brain. We were not unmindful of our earlier tragic experience in ligating the superficial veins, but this tumor looked far less vicious from the surface. After the tumor was circumvented by ligatures, extirpation was begun from the cyst forward. The cortex was first incised below the tumor in order to get the entering arterial trunks.



Fig. 17 (case 5).—Ventriculogram; a lateral view of the normal side.

A dense mass of intertwined serpentine red vessels of more uniform size was encountered.

A detour of the incision was made downward, and in this way the vascular mass was divided. Three fair-sized arteries were isolated near their entrance into the cluster of vessels. After ligation of the arterial supply, the vascular tumor was removed without difficulty. Bleeding was entirely stopped when closure was begun. However, despite a prompt recovery from the anesthetic, the patient died six days after the operation from a slowly developing intraventricular hemorrhage. During the operation the opening into the lateral ventricle had been carefully packed to preclude bleeding into it.

Necropsy showed three branches of the left middle cerebral artery clipped at the margin from which the tumor had been excised. Had it not been for the

Epileptic attacks appeared soon after the sensory and motor symptoms. They were initiated with numbness in the left arm and leg and a drawing sensation in the left side of the face, but consciousness was not lost. The attacks usually came while he was asleep and awakened him. A painful headache always followed. In some of the attacks, only part of the left side was involved. The epileptic attacks steadily increased from two or three a month in 1920 to fifteen a month. The later attacks began with numbness and stiffness of the fingers of the left hand and the toes of the left foot. The right side was never involved. Diplopia appeared recently. During the past three years the vessels over his face and head, particularly on the right side, have become much larger and more conspicuous.

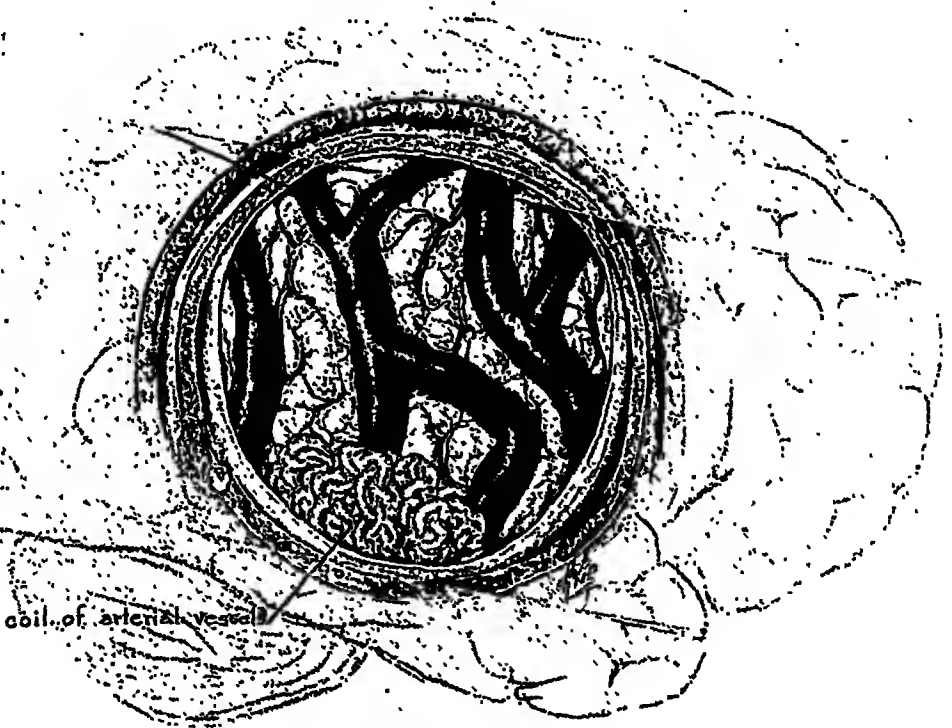


Fig. 20 (case 6).—Drawing of aneurysm as seen at operation. The interlacing vessels in the subdural space are clearly arterial. The large veins on the cortex of the brain drain the lesion which has doubtless extended into the brain.

*Examination.*—Over the occipital region of the right side was a diffuse bulging mass about 5 by 5 cm. but without sharply defined boundaries; it pulsed strongly with each heart beat. The superficial temporal, posterior auricular and occipital arteries were tortuous, much enlarged and easily visible. When all three of the arteries were compressed, the swelling in the scalp subsided and ceased to pulsate. A bony opening could be palpated just mesial to the right mastoid process and in the normal position of the mastoid vein. This opening, which also showed clearly in the roentgenogram, was about 1 by 1 cm. in diameter. Another small opening in the right frontal region was all that remained of a gradually closing decompression (performed ten years before). When the patient stooped, the veins

spells occurred once or twice a week. Limitation of vision to either side was not noticed at that time. In 1916, a decompression and puncture of the corpus callosum were performed at the Mayo Clinic. The patient was benefited for a short time, but the symptoms gradually returned.

In 1918, while on duty in France, he fell from a horse; a severe headache developed, but lasted only for several days. Craniotomy was performed at the Mayo Clinic in 1920. At that time, a choked disk was reported, and at the opera-



Fig. 19 (case 5).—Low power microscopic view of the network of vessels in the so-called angioma. These vessels vary tremendously in size and in the thickness of their walls, some contain elastic tissue of irregular strands; others do not. There is much thrombosis and irregular thickening of the intima.

tion, unusually large cortical vessels were noted. For the past six years, he has steadily become worse. His vision has steadily diminished; since 1920, he has been unable to see to the left side (left homonymous hemianopsia). The sense of pressure in the head, and particularly in the right temple, has become more and more intense. Numbness and weakness in the left hand, arm and leg began about 1921, and have gradually increased.

vein, a vein of corresponding size entered, filling the opening, and carried the blood from the vascular tumor. The angioma was dissected from the scalp and its entering arteries carefully marked for later study. The huge vein was carefully ligated at the bony opening with a transfixion suture of silk. Immediately after the operation, each vessel was carefully traced. The occipital artery passed directly into the big mastoid vein. This continuity was demonstrable by a probe which passed without interruption from the artery into the vein. Likewise a probe in the posterior auricular artery passed directly into the occipital artery just before it entered the big mastoid vein. A third small artery; presumably a branch of the superficial temporal, could not be traced accurately. There was, therefore, an arteriovenous fistula between the occipital artery and the mastoid vein and another interarterial fistula between the posterior auricular and the occipital arteries. The position of the great mastoid vein suggested that it entered the lateral venous sinus; it, therefore, seemed probable that the external arteriovenous fistula was separate and distinct from the arteriovenous aneurysm within the cranial chamber. Whether they were in communication through the lateral sinus could not be determined.

*Second Operation.*—July 20, 1926: The patient's signs and symptoms had been unchanged after the external operation. Feeling that an attack on the intracranial aneurysm would be too hazardous, a large right subtemporal decompression was performed in order to relieve the intracranial pressure. It was hoped that the patient might be relieved, at least to the extent of stopping the headaches and preserving the vision which was being menaced by a high papilledema.

When the dura, which was excessively bloody, was cautiously opened, several tortuous vessels lying in the subdural space were found attached to the inner side of the dura. Most of these vessels could be stripped away from the dura, but others entered it and had to be ligated. These extremely tortuous vessels were red and pulsated strongly. All that were visible were clearly arterial channels.

These arteries, which formed free loops in the subdural space, could be compared only to a tangled mass of angle worms; they were also about that size and fairly uniform. This vascular tumor was situated along the posterior part of the temporal lobe. Everywhere this part of the brain was completely hidden from view. Three tremendous veins emerged from this cluster of vessels. A fourth vein of about the same size paralleled the anterior part of the decompression and could not be seen to enter the angioma. Pulsation could be seen and a thrill palpated in these veins.

When the vessels were freed from the dura, furious bleeding resulted. It was possible to control the hemorrhage only by a cotton pack. The next day, careful removal of the pack was again followed by arterial bleeding, though somewhat less severe. A piece of muscle then controlled it.

The headaches were entirely relieved by the operation, but the symptoms and signs have remained as before. The decompression has since bulged at times, but at other times has been sunken.

*CASE 7.—History.*—A normal looking boy, aged 14, was referred by Dr. Ralph Greene, of Jacksonville, Fla., because of jacksonian epilepsy (Oct. 27, 1926). His trouble dated back to the age of 7 years, when his mother handed him a glass of water; he dropped it and said his hand was weak and that he could not hold it. He was conscious throughout the attack. A few weeks later when cutting paper, he complained that he could not use his right hand. Three months later, when at school, he had the first convulsion. After the attack, he recalled that his tongue

of the head and face became enormous. A loud systolic murmur was heard over the entire head, but much more over the right parietal and occipital regions.

The positive neurologic observations were: high grade papilledema (6 diopters) in both fundi; hypesthesia for pain, touch and temperature over the left side of the face and of the left arm and leg; slight weakness of the left facial muscles. The patient walked with a decidedly spastic hemiplegia gait; the left hand and arm were weaker than the right; sharply defined and complete left homonymous hemianopsia was present.

The corneal reflex was less active on the left; the knee jerks, biceps, triceps and achilles reflexes were exaggerated on the left; there was ankle clonus on the left; the Babinski sign was negative.

A roentgenogram showed a circular opening (1 by 1 cm.) in the occipital bone just mesial to the right mastoid process.

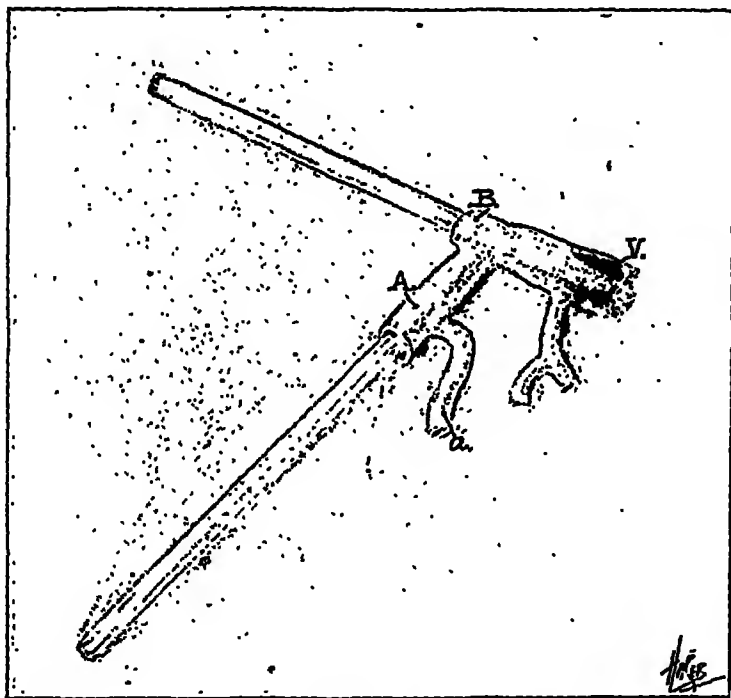


Fig. 21 (case 6).—Arteriovenous aneurysm of the scalp. The upper glass rod passes from the occipital artery into the mastoid vein (*V*). The posterior auricular artery (*A*) also is seen passing into the occipital artery near its junction with the mastoid vein. The mastoid vein entered a hole as large as one's finger to the left of the mastoid process. The superficial temporal artery (?) enters at the line of communication between the artery and veins.

*Operation.*—June 20, 1926: Since the extensive pulsating mass in the left occiput seemed to be dependent on the patency of the superficial temporal, the posterior auricular and the vertebral arteries, these were first ligated, although it was evident that the intracranial lesion (presumably also an arteriovenous aneurysm) was much more extensive, since there was hemianopsia, partial hemianesthesia and hemiplegia. The mass of vessels in the scalp was carefully dissected, and at the time the branches of the external carotid artery were exposed for ligation. All three of the vessels entered the extracranial vascular mass, and through the large, bony opening which corresponded in position to the mastoid

A diagnosis of tumor or aneurysm was made, more probably the latter because of the old history of a cerebral hemorrhage and with so little progression of signs or symptoms over a period of seven years.

A filling defect nearly obliterated the anterior part of the body of the left lateral ventricle. In the background of air, a linear calcified shadow was clearly visible, whereas in the roentgenogram without air, this shadow could not be seen.

*Operation.*—On Oct. 29, 1926, left craniotomy was performed. When the dura was exposed, a localized bluish swelling was evident toward the mesial part of the bony defect. The dura over this region had been unusually bloody; it was also thinner than elsewhere. The localized bulge was due to an underlying venous dilatation which appeared to come out of the brain tissue and which passed into a large vein that coursed mesially to the superior longitudinal sinus. It corresponded in position with the rolandic vein, which it undoubtedly represented. A second smaller vein passed downward from the mass to the sylvian vein. The large rolandic vein was distinctly red, and through its thin walls the pulsing red blood could be seen rhythmically mixing with the darker venous blood. No other enlarged veins were present on the surface of the brain. Palpation of the brain revealed an indurated area beneath the face area, but no attempt was made to expose the underlying tumor or to treat the lesion in any way. Its position in the important part of the leading cerebral hemisphere precluded any further effort.

A year later, his condition was practically unchanged.

*CASE 8.—History.*—A well nourished man, aged 35, in good general health, complained of generalized convulsions (May 5, 1925). His first attack had occurred fourteen months earlier. It was described as a generalized convulsion which came without warning and lasted about half an hour. He frothed at the mouth, bit his tongue but did not have incontinence of urine. The attack came on during sleep. A few hours later, he had another attack which seemed to be similar to the first, and two hours later another. Three months later, he had another attack at dinner, and was told that his left side had been rigid (probably incorrect). This attack lasted from twenty to thirty minutes. Additional attacks occurred six, ten and fifteen months later. Unilateral features were not noted in any of them except the one just quoted, but he has been told that his head usually turned to the right. There was no history of trauma.

*Neurologic and Physical Examinations.*—The results of the neurologic and physical examinations were negative. The Wassermann reaction of the blood was negative.

The ventricular system was dislocated to the right side, indicating a cerebral tumor on the left. The ventricular fluid was normal.

*Operation.*—On July 21, 1925, left craniotomy was performed. Five greatly dilated and somewhat tortuous veins stood out in strong relief on the surface of the brain. The rolandic and sylvian veins formed a relatively enormous continuous channel from the sylvian fossa to the superior longitudinal sinus. An almost equally large offshoot of the sylvian vein paralleled the rolandic vein and entered the longitudinal sinus, and two other branches of similar size passed downward from the sylvian vein to enter the transverse sinus. The latter veins, running closely together, formed en route a plexus over the temporal lobe. The red blood could be seen swirling in these veins with each pulse beat and mixing with the darker venous blood. The arteriovenous connection was deeper in the brain and could not be seen or palpated. The wound was closed without any attempt to treat the aneurysm.

*Second Operation.*—Two weeks later, the left common carotid artery was exposed under local anesthesia. After several transient compressions of the carotid

felt queer and that he could not swallow. It was observed that his right hand was drawn in the convulsion. A second convulsion occurred a year later; it resembled the first. A month later, the right side suddenly became completely paralyzed. Though he was unable to talk, he understood everything. There was some fever for three or four days and severe headache. A week later, the function began to return in the leg and arm, and in three weeks speech began to return. In three or four months, his speech was again normal, but there has since remained a slight residual weakness of the arm and leg. Further symptoms did not appear until two weeks before he came to the Johns Hopkins Hospital

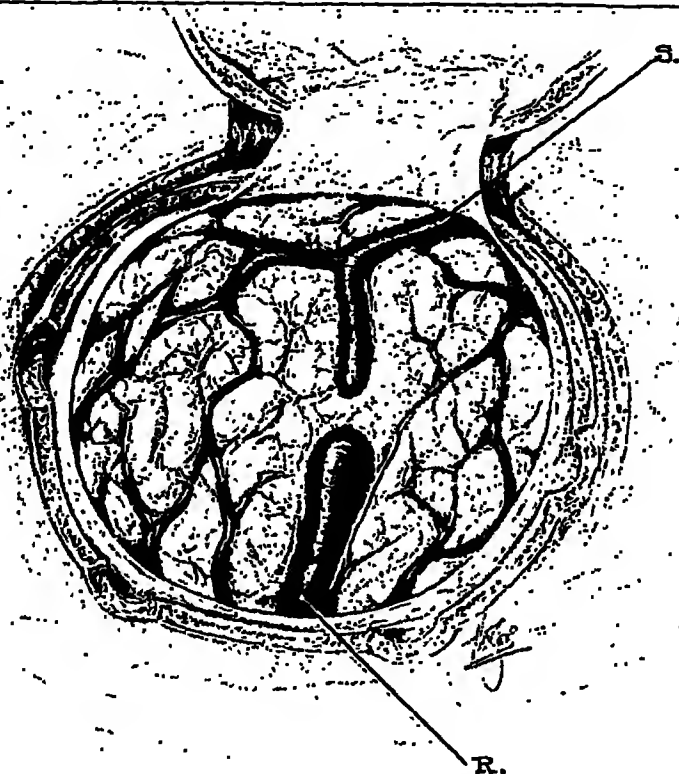


Fig. 22 (case 7).—The large rolandic vein can be seen coming directly out of the brain and has arisen from the vascular mass situated beneath. Arterial blood could be seen pumping into it. It will be noted that it has no connection with the group of veins below and which also comes out of the depth of the brain. The convolutions separate these two ends of the vein. The lower branch is continuous with the sylvian vein which is also large.

(October, 1926), when another attack began in the right hand. He had headaches only after attacks. There was no history of trauma.

**Examination.**—The neurologic examination showed the following positive symptoms: definite weakness of the facial muscles, the right hand, arm and leg; some atrophy of the right side; increased deep reflexes on the right; no ankle clonus, and a positive Babinski sign on the right.

The roentgenogram was negative. The Wassermann reaction of the blood was negative.



Pagan, of Washington, D. C., because of deforming veins of the scalp. Since early childhood (at least since she was 2 years of age), a lump had been present in the midline of the scalp and between the parietal eminences. It had always pulsated, but had been soft and painless. It had not given her any trouble, and had not grown in later years. Nine years before, when her first child was born, a lump, thought to be a big vein, appeared in the middle of the forehead. This swelling grew forward and became larger spasmodically; during each of seven pregnancies, it increased in size until it overhung the bridge of the nose and extended over to the inner canthus of each eye. Many other large tortuous veins



Fig. 24 (case 8).—Ventriculogram showing the small left anterior horn as compared with the normal on the right.

filled the scalp and became steadily larger until they began to encroach on the outer canthus of both eyes. The patient again became pregnant and was anxious about the vein increasing in size at the time of delivery. There had been no signs of intracranial pressure, though intermittent general headaches had been present for four or five years. On one occasion she had had an attack of numbness involving the right hand and lasting two weeks, but consciousness was not lost. There was no motor weakness during the attack, or at any other time. Noises in both ears had appeared recently and were somewhat annoying.

without subjective or objective noticeable change, the artery was ligated just below the junction of the internal and external carotid arteries. Manometric readings of the spinal fluid were made at the time of compressions of the internal carotid artery (lumbar puncture was performed at this time). With each temporary closure of the common carotid artery, the pressure of the spinal fluid fell from 240 to 215 mm. The pressure returned to its former level when the arterial compression was released. The blood pressure rose from 104 to 110 immediately after the ligation.

It should be noted that for several days before the ligation, the carotid artery was compressed on many occasions by pressure on the neck and without symptoms; the results indicated that the operative ligation would probably be safe.

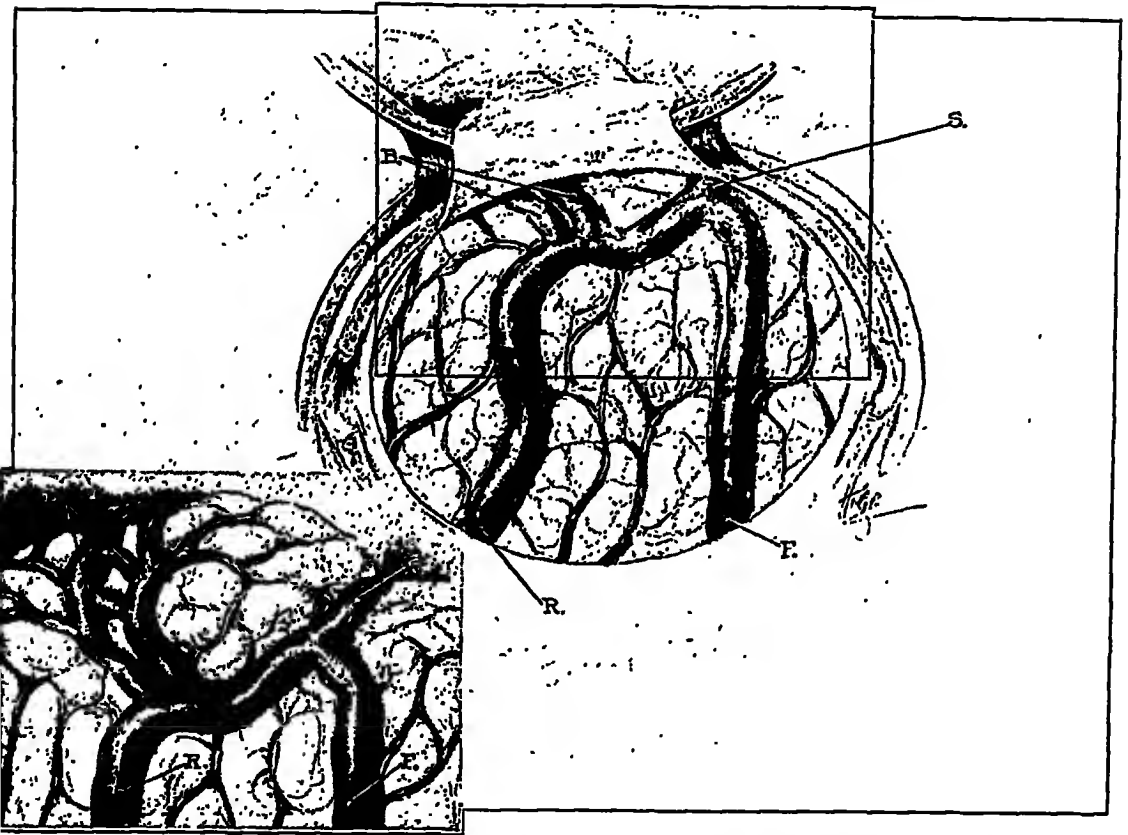


Fig. 23 (case 8).—Showing the distribution of the large distended veins on the surface of the brain and also the cluster of veins over the temporal lobe. Arterial blood could be seen pumping into these tremendous channels. As this aneurysm involved the most important part of the brain no attempt was made to treat the aneurysm directly. The left internal carotid artery was subsequently ligated. *R* indicates rolandic vein; *S*, sylvian vein; *F*, frontal vein; *B*, veins to lateral sinus.

The patient has remained free from both petit and grand mal attacks to date (two and a half years). There have been no untoward symptoms as a result of the closing of the common carotid artery.

*Extracranial Arteriovenous Aneurysm—the Prototype of the Intracranial Lesion.*—A well nourished, healthy woman, aged 29, was referred by Dr. A. E.

therefore, eliminated by the test. Palpation of the veins failed to disclose an arterial pulsation. A slight murmur could be heard over the veins when examination was made with a stethoscope. A thrill could be definitely made out over the large median vein and in other veins near the tumor. The greater the distance from the tumor, the less distinct the thrill became. The degree of pressure must



Fig. 26.—Arteriovenous aneurysm of the scalp which doubtless had intercranial extensions since the patient had localized sensory involvement of the right hand at one time. This lesion is a prototype of the intercranial aneurysm shown in figure 20. A localized mass posteriorly corresponds with the so-called angioma.

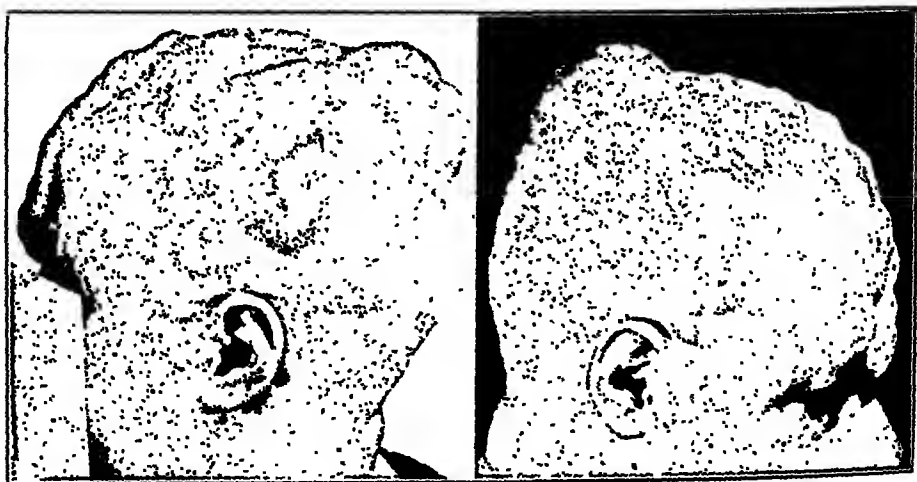


Fig. 27.—Same as patient in figure 26.

be just right to elicit the thrill. All of the veins were easily compressed. The tumor mass itself gave a strong expansible pulsation. The tumor was fairly soft and partly compressible, giving the impression of a mass of angle worms. When the mass was compressed firmly, it became painful and induced headaches. Compression could not be tolerated for more than a few minutes, nor could a number

*Examination.*—A pulsating tumor about as large as a lemon was palpable in the midline of the head between the parietal eminences. When the whole head was shaved, this mass was easily visible. From this tumor, as from the hub of a wheel, a number of enormous, tortuous veins coursed posteriorly, laterally and anteriorly (fig. 27). Pressure on the jugular veins promptly caused them to become tight and much fuller. Pressure on certain veins caused the distal portion to collapse, but the collapsed portion nearly always filled up slowly from collateral channels; when the collateral channels also were compressed, the distal part of

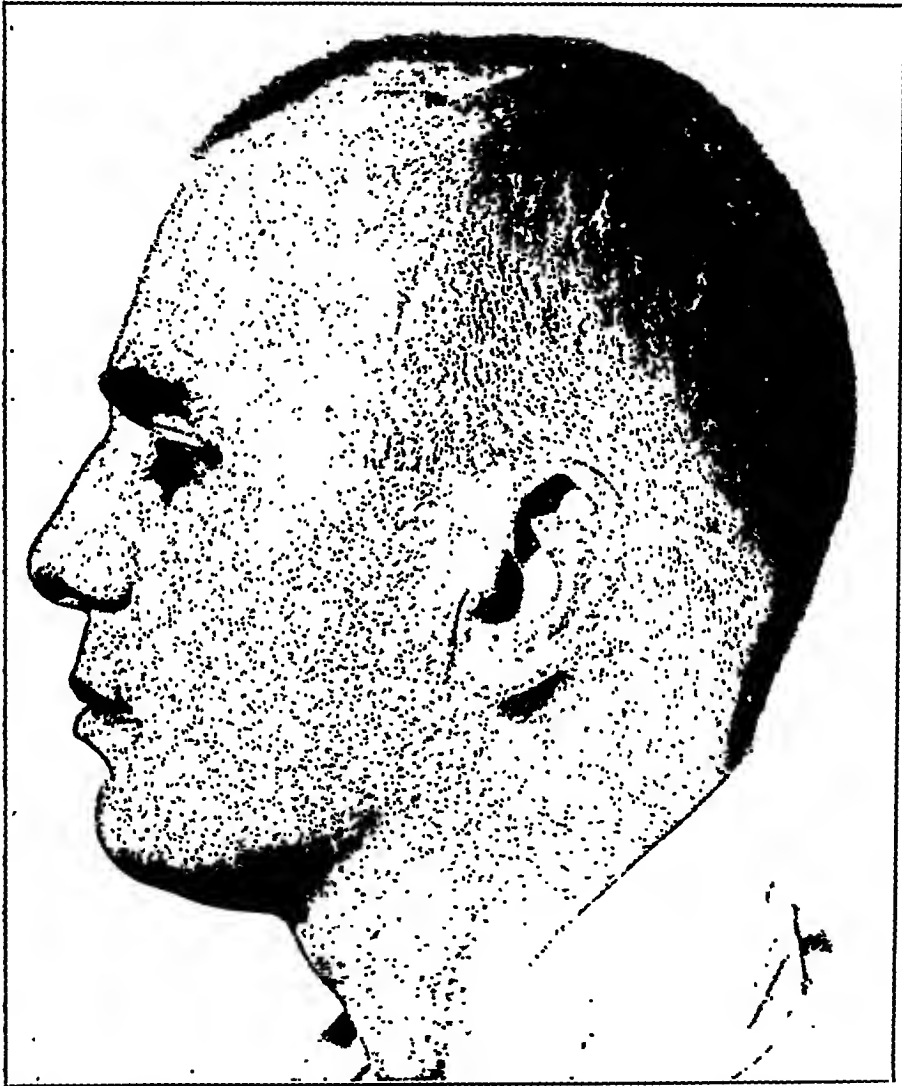


Fig. 25 (case 8).—Patient after ligation of the internal carotid artery in the neck.

the veins remained collapsed and did not fill (fig. 28). Particular reference is made to this point because of the large midline vein which extended to the nasion. When the collapsed venous space was palpated, it felt rough and one received the impression that there was a groove in the bone; until this test was made we wondered whether there might not be communication with the superior longitudinal sinus situated immediately beneath. The possibility of this communication was.

TABLE 1.—Analysis of Author's Eight

Case, Age, Sex*	Location of Vascular Tumor	Duration of Symptoms	First Symptom	Principal Symptoms	General Pressure Signs and Symptoms	Focal Symptoms	Röntgen- Ray Observations	Eye-grounds
I 52 ♂	Right temporal lobe	6 yr.	Convulsion (general)	Convulsions (grand and petit mal); headache (1 week); sore- ness right tem- ple (1 week)	Headache (1 week)	Head turns to left in convul- sion; some subjective numb- ness in fingers of left hand	Negative	Normal
II 19 ♂	Right parietal lobe	4 yr.	Convulsion	Jacksonian convulsions often followed by weakness of left hand	None	Jacksonian convulsions beginning in left side of face	Negative	Normal
III 35 ♂	Cerebellar left verte- bral artery	2 yr.	Staggering gait	Staggering gait, diplopia, head- ache, dizziness, dysarthria; mental im- pairment.	Headache; choked disk; hydrocephalus	Staggering gait, Romberg, deafness	Negative	Choked disk
IV 47 ♂	Fronto- parietal right	6 yr.	Focal con- vulsions	Convulsions; motor loss on left side	None	Left hand, arm and leg involved in convulsion; motor weakness left arm	Extensive shadows in right fronto- parietal region	Normal
V 48 ♂	Parieto- occipital right	10 yr.	Convulsion	Convulsions; cerebral hemor- rhage, moody and forgetful	None, except during cere- bral hemor- rhage from which he recovered	Left side in- volved in attacks; left paresis, anes- thesia, and hemi- anopsia after cere- bral hemorrhage, later disappeared	Negative	Normal
VI 31 ♂	Temporo- occipital	15 yr.	Transient visual dis- turbances	Headache, con- vulsions, hemi- plegia, hemian- esthesia, hemi- anopsia, diplopia	Choked disk; headache	Hemiplegia, hemi- anesthesia, hemi- anopsia, focal convulsions (left side)	Large cir- cular hole in right occiput	Choked disk
VII 14 ♂	Parietal	7 yr.	Attack of weakness in right hand	Convulsions (Jacksonian); weakness right side of body; symptoms for cerebral hemor- rhage on one occasion	None	Weakness right side of face, right arm and leg; at- tacks beginning in right arm; motor aphasia and hemiplegia after cerebral hemorrhage	Linear calcified shadow	Normal
VIII 35 ♂	Left parietal	14 mo.	Convulsion	Convulsions	None	Head turns to right	Negative	Normal

\* In this table and the following tables, ♂ indicates male; ♀, female.

of veins be compressed at one time without causing pain and headache—doubtless for the same reason. Temporary occlusion of the veins caused the central tumor to become full and tight.

The roentgenogram showed large grooves of the middle meningeal artery on both sides; both grooves extended to the midline and appeared to end directly beneath the tumor of the scalp, otherwise the roentgenogram was negative.

The results of the neurologic examination were negative. The Wassermann reaction of the blood was negative.

A diagnosis of arteriovenous aneurysm of the scalp was made. The large channels of both middle meningeal arteries and the focal numbness of the hand made it seem probable that there was an intracranial extension of the aneurysm.

*Operation.*—The tumor itself was not removed, for intracranial extension was feared, because of the numbness of the hand which had been present for two



Fig. 28.—The collapse of the vein over the forehead when the arterial supply is cut off from the vascular mass. The venous channels then become greatly sunken.

weeks. The superficial temporal, internal maxillary and occipital arteries were ligated on both sides of the neck. On the left side, the external carotid artery was also ligated at its origin. After ligation of the arteries, the veins responsible for the tumor on the forehead were ligated. The veins responsible for this part of the swelling had previously been determined by compression with the fingers. The disfiguring part of the venous bed at once disappeared and has not returned. The redundant part of the skin disappeared and no sign of the old deformity remained. A few days after the operation, all of the veins in the scalp became hard and tender and were no longer compressible. Apparently they had thrombosed, and when the patient was seen six months later, all trace of them had disappeared. The central tumor mass had greatly diminished in size and no pulsation could be detected. The tinnitus had ceased. The patient had been well in every respect.

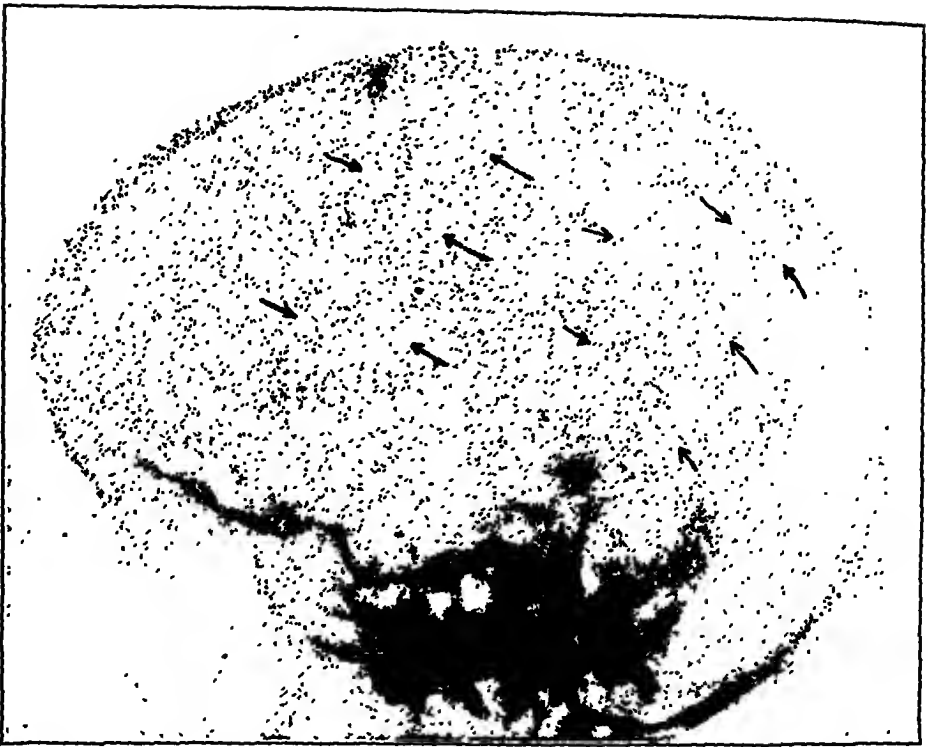


Fig. 29.—Greatly enlarged meningeal grooves, both right and left, directed toward the vascular bed of this aneurysm (interior set of arrows). The posterior set of arrows show the greatly enlarged venous channels in the skull providing exit for the blood leaving the vascular tumor, i. e., to the lateral sinuses.

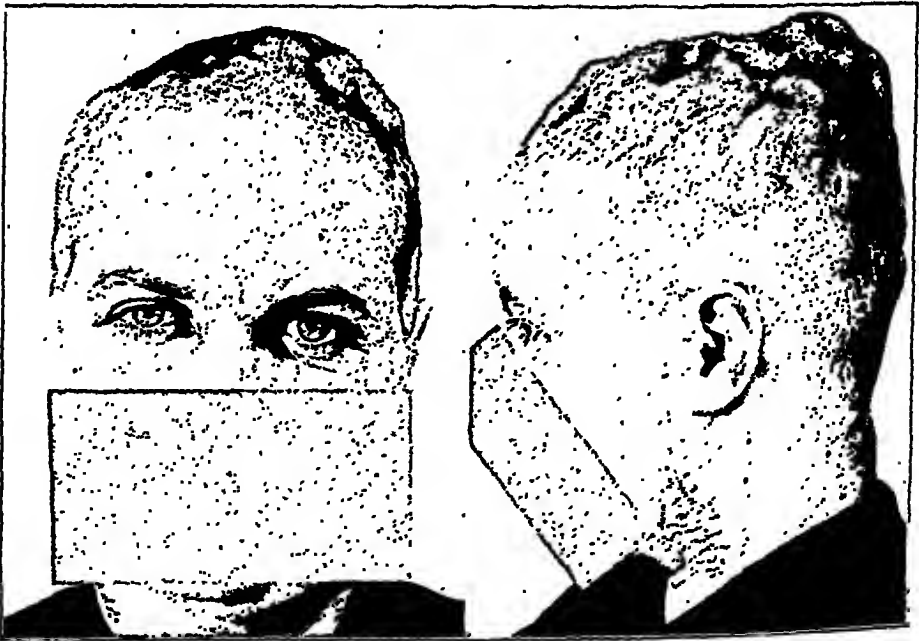


Fig. 30.—Result two weeks after the operation at which the occipital, posterior auricular, internal maxillary and superficial temporal arteries were ligated on both sides, and in which the venous channels were ligated at the two points indicated by the pressure of the fingers in figure 28. Several months after this photograph was taken all the veins had subsided and the pulsation in the arterial mass had ceased.

# Cases of Interventricular Aneurysms

Head-ache 1 week only	General Epilepsy	Focal Epilepsy Head turns to left	How Diagnosed Ventriculo- graphy and exploratory	Diagnosis before Operation or Autopsy Tumor of the brain	Operations and Observations Anomalous branch of right middle cerebral artery supplied vascular mass; after its ligation, mass of venous vessels collapsed	Condi- tions at Securesy Living	Remarks Patient has had but one attack since op- eration (3½ years); never had headache; general health excel- lent
None	..	.. begins in left face and arm	Ventriculography	Tumor of the brain	Mass of serpentine ves- sels with large emerg- ing veins; attempted extirpation; vessel burst between the liga- tures	.....	Patient died of hemor- rhage
	None	None	Neurologic signs of local- ization; cere- bellar explora- tion	Tumor of the brain	(1) Cerebellar explora- tion; (2) ligation left vertebral artery	Living	Patient's general pres- sure and neurologic signs and symptoms largely disappeared, but mental changes persisted
None	..	.. left arm	Röntgeno- gram	Aneurysm of the brain	(1) Exploration of men- ingium; (2) internal carotid artery ligated	Living	Attacks returned after a year's absence fol- lowing operation; the shadow in the rönt- genogram was the im- portant diagnostic sign in this case
None	..	..	Ventriculo- graphy	Tumor or aneurysm (cause of cerebral hemor- rhage)	Ligation of vascular tumor	Shows arterial trunk from middle cerebral supplied tumor	Cerebral hemorrhage from the vascular mass
Severe	..	..	By external arteriovenous vascular bed	Arterio- venous aneurysm	(1) Extracranial arterio- venous aneurysm (dis- sected out); (2) mass of angle worms in tempo- ro-occipital region; big veins (in cortex) with arterial pulsation	Living	Two separate arterio- venous aneurysms present, one in the scalp, the other in the brain
None	..	+	Ventriculo- graphy, history and exploration	Tumor or aneurysm	Big venous dilatation in which arterial blood could be seen	Living	Patient gave history of a cerebral hemorrhage, one year after first symptoms
None	+	Head turns to right	Ventriculo- graphy	Tumor of the brain	(1) Large distended ro- und and sylvian veins; arterial blood seen (through wall of vein) to be pumping into venous blood; venous plexus over temporal lobe; (2) internal carotid artery ligated	Living	Has had no attacks to date (2½ years)



## THE GROSS APPEARANCE OF ARTERIOVENOUS ANEURYSMS

The venous trunks draining the aneurysms (when located in the cerebral hemisphere) nearly always connect with the external venous circulation through the rolandic and sylvian veins, and when these form a continuous channel, as they usually but not always do, both show the maximum effect of the arteriovenous connection. This is evidenced by their dilatation throughout their course. The degree of involvement of the contiguous veins varies in individual cases; at times other nearby veins may be almost unaffected. In a single case, the venous outlet was through the internal venous system (Steinheil); one small vein of Galen and the great vein of Galen were dilated and tortuous throughout their course to the sinus rectus. In addition, a sacculated aneurysm with a long pedicle was present on the vein of Galen.

Because the external venous system carries the outflow of blood from most of the arteriovenous connections, the characteristic venous changes are on the surface of the brain. This makes it possible to detect these cases so easily at operation. And since the veins are free from all accessory coverings, it is also possible to see through their walls and detect the pulsing red, arterial blood against a background of black venous blood. This opportunity does not exist elsewhere in the body. So far as I am aware, attention has not been directed to this point—so essential to the diagnosis—heretofore.

In many of the cases of arteriovenous aneurysms located in the cerebral hemispheres, there are congenital abnormalities of the venous system on the exterior part of the hemisphere. In one case, the rolandic vein arose directly out of the brain substance, having its origin in the aneurysm. In two other cases, the rolandic vein did not exist as a well defined venous channel.

The degree of venous engorgement is dependent on the size of the arterial supply and on the size of the mass of vessels, or rather on the size of their lumina, forming the arteriovenous communication. A large angioma with many vessels takes some of the brunt of the arterial force off the venous channels of exit. A small angioma or a short connecting link throws all the arterial force directly into the veins. The smaller the artery and the smaller the lumen of the arteriovenous communication (i.e., the larger the number of vessels intervening between the artery and veins), the smaller will be the venous channels which drain the aneurysm. And conversely, the larger the artery and the larger the lumen of the arteriovenous connection (i.e., the smaller the mass of vessels between the artery and vein), the greater will be the effect on the veins emerging from the aneurysm. Many large veins, therefore, indicate a small angioma or a free end to end communication between an artery and vein. Smaller veins indicate a larger angioma and an arteriovenous

In retrospect, there is reason to believe that removal of the mass might have been safely performed without ligation of the branches of the external carotid. The result, however, would not have been different.

#### SEX AND AGE AND TIME OF APPEARANCE AND DURATION OF SYMPTOMS IN CASES OF ARTERIOVENOUS ANEURYSM OF THE BRAIN

In the literature, twelve of the cases of arteriovenous aneurysm of the brain reported occurred in men and eight in women. Curiously, the eight patients in the cases reported in this paper were men, but there seems to be no reason to lay emphasis on this point or to expect any differences due to sex.

The time of appearance of convulsions or the other more occasional symptoms is one of the most surprising features of this lesion. Being surely of congenital origin, it would be logical to expect symptoms soon after birth. Data on this point are available for eighteen of the thirty cases as follows: The first symptoms appeared in seven patients between the ages of 1 and 10; in three patients between 11 and 20; in three patients between 31 and 40; in five patients between 41 and 50; there was no record of first symptoms for patients between 21 and 30 years of age.

In 44 per cent of the patients, therefore, the first symptoms did not appear until after the age of 30 and in 30 per cent, symptoms began after the fortieth year. The latest time of appearance was at the age of 48.

The duration of symptoms ranged from a few hours to fifty years. In four of eighteen cases, symptoms had been present for more than twenty years.

#### LOCATION OF INTRACRANIAL ARTERIOVENOUS ANEURYSMS

The aneurysms are located in almost every part of the brain. Three are in the cerebellar region (Leunenschloss,<sup>27</sup> Znojensky,<sup>28</sup> Dandy). In one case (Znojensky) there were two separate and distinct aneurysms: one in the right cerebellar lobe, the other in the cerebral hemisphere. In two instances, there were arteriovenous aneurysms in the scalp, apparently independent of the intracranial lesion (Mihlsam, pulsating exophthalmos; Dandy, occipital artery and mastoid vein).

An overwhelming proportion of the aneurysms are located in the paracentral region and have arterial connection with a branch of the middle cerebral artery. In two cases, the corpus callosal artery suggested the arterial connection (Deetz,<sup>29</sup> Steinheil<sup>30</sup>).

section. The walls are at times thin, suggesting veins, and others alongside are thicker, suggesting arteries. The intima may be narrow, but frequently it is greatly thickened and at times irregularly so. Many vessels are entirely occluded by thrombus formation. The elastic fibers are shown in special stains to be present in the intima of many vessels but not in others. Rarely is the elastic tissue a well defined layer; usually a strand is present here and there. The media is usually poorly developed, with much hyaline degeneration or calcification. These changes, while doubtless varying considerably in detail, are essentially similar in all microscopic reports in the literature. They indicate abnormal, poorly developed vessels with debilitated walls, which render the person the victim of vascular rupture long before the allotted time for normal vessels. The extensive thrombosis has been commented on by several authors (Emanuel,<sup>32</sup> Therman,<sup>33</sup> Leunenschloss,<sup>27</sup> Astwazturoff,<sup>9</sup> Kaiserling<sup>30</sup>). It is doubtless one of the important reasons for the progression of the lesion in the later years of life. Each thrombosed vessel throws an additional strain on the venous system and on the angiomatous mass. Doubtless it is this added strain which is also responsible for many of the hemorrhages. The intercommunication of the vessels within the vascular nest has been described. I have been unable to learn whether or not this was true in case 2 which came to necropsy, for the mass was mutilated during its removal. Simmonds<sup>16</sup> reported evidence of canalization of thrombi.

#### SIGNS AND SYMPTOMS OF ARTERIOVENOUS ANEURYSM OF THE BRAIN

(a) *Convulsions*.—With four exceptions, the first symptom in this group of cases was a convulsion, and most of these (all but two) were of the jacksonian type. The starting point of the seizures, i.e., the aura, when present, varied with the exact point at which the motor or sensory tracts were involved. It is, of course, not necessary that the attacks show the jacksonian march; at times even the focal or unilateral character of the attacks may be none too clear, though probably in all cases there will at least be turning of the head to the opposite side. Jacksonian attacks are present only when there is a direct infringement on the motor tracts. Those aneurysms at a distance from the motor tracts will give less conspicuous unilateral signs in the attack, and usually no aura. In two of the cases reported here, there were no warning signs (aura). In both of the cases without jacksonian convulsions the head

32. Emanuel, C.: Ein Fall von Angioma arteriale racemosum des Gehirns, Deutsche Ztschr. f. Nervenhe. 14:288, 1898.

33. Therman, E.: Ein Fall von Angioma racemosum cerebri, Arch. a. d. path. Inst. d. Univ. Helsingfors 3:67, 1910.

communication which is relatively well compensated, i. e., nearer the function of the capillary system. Doubtless there are many smaller arteriovenous aneurysms with a small arterial inlet and relatively small veins of exit which could not be established as abnormal. A thrill could not be felt in these, nor could arterial blood be seen pumping into them. There have been several cases at the Johns Hopkins Hospital which showed definite vascular abnormalities and which were thought to be arteriovenous aneurysms, but these have been excluded from all consideration because the absolute evidence was lacking.

Kaiserling's<sup>30</sup> case and case 1 in my series are excellent examples of excessively large and tortuous veins which result when no barrier is interposed between an artery and a vein. In Kaiserling's case, a tortuous elongated artery could be seen emptying directly into a huge venous chamber. In case 1, a short anomalous branch of the middle cerebral artery, and with normally thick arterial coats, abruptly passed into a vein. The transition between the thick arterial and the thin venous coats was clearly seen during the inspection of the vessel. Reid's case<sup>31</sup> of an arteriovenous aneurysm between the subclavian artery and veins in the neck seems in every way an exact duplicate of this case in the brain.

A mass of vessels forming the connection between the artery and veins, i. e., the so-called angioma, when such is present, is usually in the depths of the brain, but this is not necessarily true. In case 6, the mass was external, at least in large part. The gross character of the mass of entwined vessels is also variable: some look exactly like arteries, some like veins, and some like a combination of arteries and veins.

The arteries supplying the mass of vessels have always been larger than normal; some have been very tortuous (Deetz,<sup>29</sup> Simmonds,<sup>3</sup> Kaiserling<sup>30</sup>). In the only case of my series in which the artery was observed, the middle cerebral artery was enlarged all the way to the internal carotid artery. It was not tortuous, nor was its enlargement excessive—perhaps from one-third to one-half larger than the corresponding vessel of the opposite side (fig. 16). The arterial change, while always definite, is never comparable to that of the veins, which is really the characteristic part of the picture of arteriovenous aneurysm.

#### HISTOLOGIC APPEARANCE OF THE VESSELS IN SO-CALLED ANGIOMA

Steinheil<sup>10</sup> and was present in two of the cases in my series, one permanently, the other only transiently after a cerebral hemorrhage. Simmonds<sup>16</sup> reported blindness in one eye and loss of smell and taste. The reflexes on the contralateral side of the body are, of course, always increased when a motor weakness exists; often ankle clonus and usually a positive Babinski are also present under the same conditions. Deist's patient had a positive Babinski sign, even though motor weakness was not apparent.

Mental changes have been uncommon. Steinheil's patient became demented. One of the patients in my series became moody and was forgetful after recovery from a cerebral hemorrhage.

(d) *Cardiac Changes*.—Hypertrophy of the heart has been shown to occur in dogs after the production of arteriovenous fistulas (Reid,<sup>5</sup> Holman<sup>7</sup>). Some of the cases reported by Reid and Holman also showed cardiac hypertrophy and even decompensation, for which they assumed the arteriovenous fistula to be responsible. Since enlargement and tortuosity of the arteries always follow a fistula, it is easy to believe that the heart too must suffer. Holman produced measurements to indicate that the size of the heart was actually reduced after the cure of an arteriovenous fistula. Emanuel,<sup>32</sup> Isenschmid<sup>26</sup> and Laves<sup>35</sup> found cardiac enlargement in their cases and attributed it to the effects of the aneurysm. The heart was not found to be enlarged, or its function disturbed in any of the cases reported here.

(e) *Signs and Symptoms of General Pressure*.—In only seven of the thirty cases was there a history of headaches (Mühsam,<sup>12</sup> Simmonds,<sup>16</sup> Eiselsberg,<sup>13</sup> Emanuel,<sup>32</sup> Dandy, [three]). This is noteworthy when the great size of the lesion is considered. The space adjustment, however, has occurred in early life and only gradual changes usually occur thereafter, excluding, of course, the always overhanging possibility of a sudden hemorrhage. In one of my patients, a man of 52, a headache had been present for only a week prior to the patient's admission to the hospital; his headache was sharply localized to the right frontal region owing to the fact that the vascular bed was in contact with the meninges. The headaches in other cases have been generalized. The patient of Campbell and Ballance and three of the patients in my series had severe headaches after each attack. Emanuel's patient was excused from military duty because of severe headaches which persisted throughout youth and finally disappeared; his head was also large.

Few examinations of the eyegrounds are reported in the assembled cases. A papilledema is reported only by Mühsam. The eyegrounds were carefully examined in all of our cases. In six, there was no change; in two, a well advanced choked disk. The pressure in one of these was due to an obstructive hydrocephalus; the cerebellar lesion had

turned away from the side of the aneurysm and eventually in each other unilateral features presented.

In a number of instances, consciousness was not lost in the attacks even when the seizure involved an entire side of the body. (Deist,<sup>34</sup> Laves,<sup>35</sup> Steinheil,<sup>16</sup> Dandy). Later, as the attacks became more severe, the other side of the body also became involved and consciousness was lost.

Indeed convulsions need not occur even though the motor or sensory areas are involved. Only two cases in which the cerebral hemispheres were involved failed to cause epilepsy (Simmonds,<sup>14</sup> Struppler<sup>15</sup>). Two cases of cerebellar arteriovenous aneurysms involving the cerebellum failed to produce convulsions (Lemmenschloss,<sup>27</sup> Dandy), but tumors in the cerebellum or the posterior cranial fossa rarely cause epilepsy,

(b) *Motor and Sensory Disturbances.*—Another important and frequent sequel of the convulsions is a transient sensory or motor paralysis. This occurred in nearly all of the cases which have been reported. Sensory or motor weakness following a convulsion is strong evidence in favor of a tumor of some kind. When the same motor involvement occurs repeatedly with such precision of attack and over a period of so many months or years and with little or no permanent progression, an arteriovenous aneurysm would appear to be the most probable lesion. The paralysis often does increase slowly in these cases, for the volume of the vascular network must slowly increase, especially in later life. It will be remembered that the degenerative and proliferative changes (calcification and thrombosis) which occur prematurely in the angiomatic mass must from time to time demand readjustments and always the volume of the network of vessels must expand in this process, thereby causing increased paralysis.

Sudden hemiplegia or hemianesthesia are the results of hemorrhage, which is so prone to occur at any age, but particularly during advancing years. Usually the paralysis disappears, in part or whole, the amount of recovery depending on the proximity of the aneurysm to the motor or sensory tracts.

(c) *Other Focal Signs and Symptoms.*—Other focal manifestations are at times present. Transient attacks of aphasia occurred in the cases of Ranzel<sup>36</sup> and Sterzing.<sup>37</sup> Homonymous hemianopsia was noted by

34. Deist, H.: Ein Fall von Angioma racemosum der linken Lobus paracentralis in seiner klinischen und versicherungsrechtlichen Bedeutung, Ztschr. f. d. ges. Neurol. u. Psychiat. 79:412, 1922.

35. Laves, W.: Ein Fall von Angioma arteriale racemosum des Gehirns, Jahrb. f. Psychiat. u. Neurol. 44:55, 1925.

36. Ranzel, F.: Zur Kasuistik kombinierter Hirnaffektionen; ein Fall von Rankenangiom des Gehirns mit tuberculous Meningitis, Wien. klin. Wchnschr. 22:1214, 1909.

37. Sterzing, P.: Ein Fall von Angioma arterial racemosum im Gehirn, Centralbl. f. allg. Pathol. u. path. Anat. 19:278, 1908.

*Roentgenologic Evidence.*—The results of the roentgen-ray examination were of great importance in two cases. In one case, a probable diagnosis of an intracranial aneurysm was made principally on the basis of the roentgen-ray examination. A series of calcified shadows covered an area roughly circular and about 5 cm. in diameter; all were beneath the surface of the brain. While most of the shadows had no unusual shape, circular or spiral, the shape of three of this group suggested calcium deposition in the walls of the blood vessels. In fact, such shadows could hardly be produced in any other lesion (excepting of course calcified blood vessels in tumors).

In a second case, a linear shadow, 1.5 cm. long, could be seen along the anterior horn of the lateral ventricle. This shadow, however, was visible only after the ventricle had been filled with air, which afforded an excellent contrast medium for the background. In a third case, a circular hole about 1 cm. in diameter, located alongside the mastoid, was clearly shown in the roentgen ray. The importance of this roentgenographic evidence, however, was minimized because it was readily palpable, being large enough to admit the tip of the index finger.

The large middle meningeal grooves (bilateral) commented on in the history of the extracranial arteriovenous aneurysm cannot be used as positive evidence because a cranial exploration was not made. As almost all of the intracranial aneurysms are located within the brain, there is little possibility of any vascular burden being referred to the middle meningeal arteries, and therefore the arterial vascular changes which are usually sought from this source in roentgenograms of the skull will be lacking. The positive roentgen-ray observations in cases of arteriovenous aneurysms of the brain will be largely confined to the calcified deposits in the abnormal vessels of the brain, or perhaps to localized areas of erosion. It is noteworthy that in two of the cases reported here, there was a localized erosion of the inner table of the skull, but the roentgenograms failed to disclose it.

#### VENTRICULOGRAPHY

The use of the air contrast medium in the cerebral ventricles is always important when the existence or even the character of an intracranial lesion is in doubt. Even though arteriovenous aneurysms only occasionally produce signs and symptoms of intracranial pressure, the lesion is one which occupies intracranial space, and therefore will usually give the positive evidence of a deformed ventricular system. Mention need not again be made of the calcified deposit which could be observed only with an air background, but such a condition is of less importance than the deformation of the ventricular system.

In two of the cases in my series in which the unilateral character of the attack was rather uncertain, the ventriculogram showed the entire

blocked the aqueduct of Sylvius. In the other case, a choked disk had been present for more than ten years. After a subtemporal decompression, the decompression was at times full and tight, again soft and even sunken. The great variations in pressure may account for the preservation of vision even with such a long-standing swelling of the eyegrounds.

Diplopia as a sign of pressure was reported only twice (Mühsam, Dandy).

(f) *Cerebral Hemorrhage*.—The premature degenerative vascular changes which have been commented on explain the frequency of cerebral hemorrhage in this group of cases. It is a fairly safe, but not absolute, rule that when a cerebral hemorrhage occurs during youth or middle age, i. e., before the time when vascular accidents are to be expected, there must be an underlying tumor or aneurysm, either of which will contribute defective vessels. In the twenty-two cases collected from the literature, nine patients, or 41 per cent, died of cerebral hemorrhage (Drysdale,<sup>38</sup> Kaiserling,<sup>39</sup> Borchardt,<sup>39</sup> Ranzel,<sup>30</sup> Simmonds,<sup>16</sup> Sternberg,<sup>40</sup> Sterzing,<sup>37</sup> Wichern<sup>41</sup> and Leunenschloss<sup>25</sup>). Only two of the eight patients whose cases are reported herewith had a cerebral hemorrhage, one known and the other presumed from the history, but both patients recovered. The probability of death from cerebral hemorrhage from these lesions is also increased because in many instances the nest of vessels frequently projects into the lateral ventricle. A hemorrhage of smaller size may develop in the tumor or the contiguous brain tissue and may not induce coma, as in one of the eight cases; the hemorrhage seemed certain because of the sudden complete hemiplegia with slow recovery. Sterzing's case is a remarkable example of the capricious character of the defective vessels in the vascular network. His patient, who died of cerebral hemorrhage at the age of 32, had suddenly developed hemiplegia with disturbance of speech (presumably due to a cerebral hemorrhage) twenty-two years earlier when 10 years old. After a slow return of function, there had been no motor change until a year and a half before death, when the same side again became paralyzed; curiously, jacksonian convulsions did not develop until after this late attack of paralysis. Childbirth was an inciting cause of the cerebral hemorrhage in Borchardt's case.

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38. Drysdale, J. H.: Report of Case, Pathological Society of London, *Lancet*, 1904, p. 96.

39. Borchardt, M.: Die chirurgische Bedeutung der Gehirnaneurysmen, *Beitr. z. klin. Chir.* 133:429, 1925.

40. Sternberg, C.: Demonstration eines Falles von Angioma arteriale racemosum des Gehirns, *Verhandl. d. deutsch. path. Gesellsch.* 7-9:308, 1905.

41. Wichern, H.: Klinische Beiträge zur Kenntnis der Hirnaneurysmen, *Deutsche. Ztschr. f. Nervenhe.* 44:220, 1912.



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In two of the cases in my series in which the unilateral character of the attack was rather uncertain, the ventriculogram showed the entire



those described in the typical cases, the diagnosis of arteriovenous aneurysm should at least always be strongly suspected.

Moreover, given sharply defined jacksonian convulsions, appearing in youth and continuing into adult life, with a gradually progressive

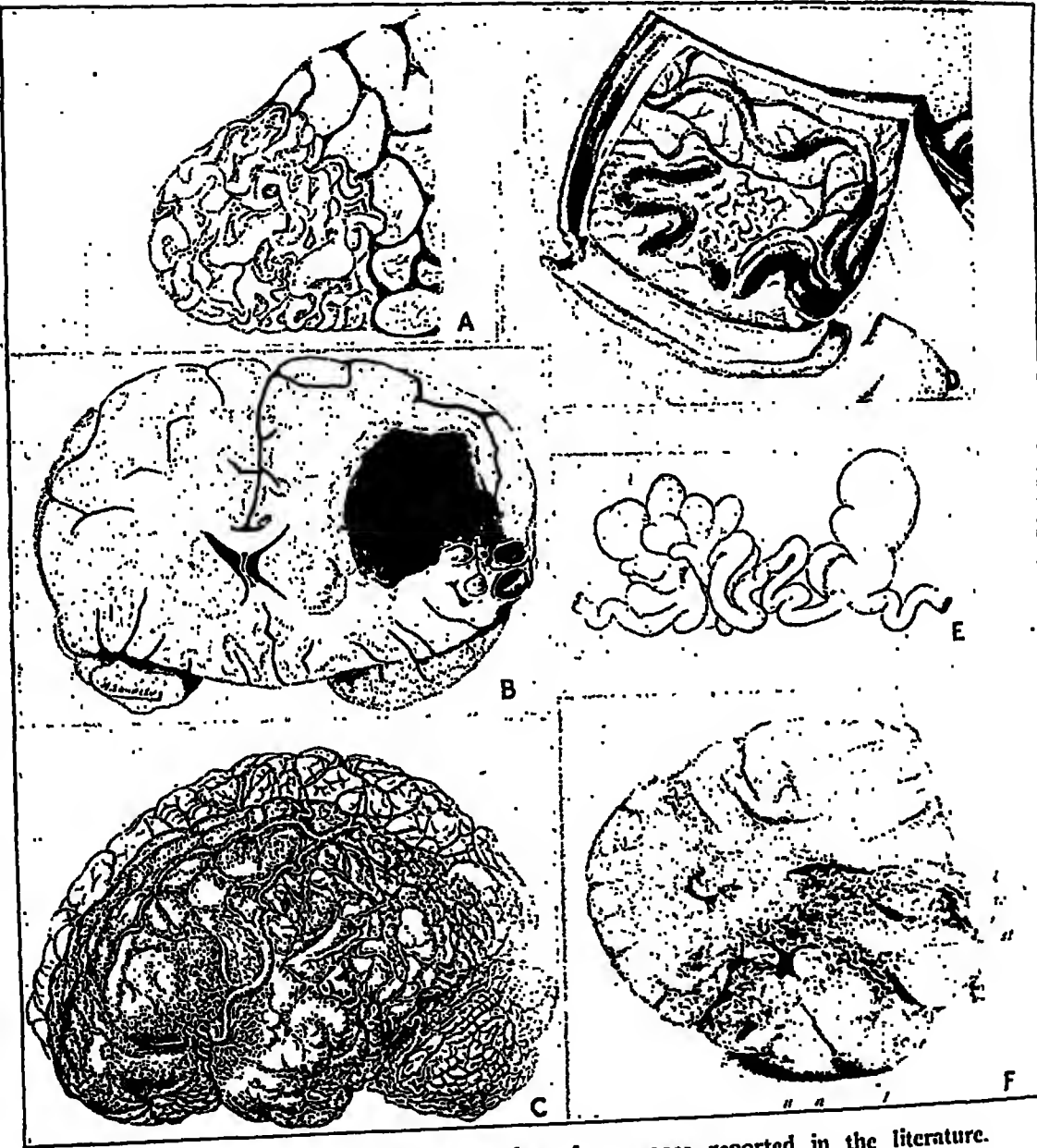


Fig. 31.—Group of specimens taken from cases reported in the literature. They show the variations which arteriovenous aneurysms may take in the brain. *A* indicates Simmond's case; *B*, Borchardt's case; *C*, Kalischer's case; *D*, Krause's case; *E*, Simmond's second case (the mass was dissected); *F*, Emanuel's case.

paralysis and then a superimposed cerebral hemorrhage such as afflicted so many of these patients, one could almost venture an absolute diagnosis of an arteriovenous aneurysm.

ventricular system to be dislocated to the opposite side. The roentgenographic changes do not, of course, make the diagnosis of an arteriovenous aneurysm; they only denote a space occupying lesion. In another case, the ventriculogram indicated a large defect communicating with a lateral ventricle. Since the patient had previously had a history of cerebral hemorrhage, the ventricular hernia was assumed to be due to the localized hemorrhage which occurred on that occasion. But this cranial defect did not indicate the location of the aneurysm or tumor which had caused the hemorrhage.

Ventriculography yields much invaluable information in cases of epilepsy. It at once separates those lesions which are space-occupying. It will also demonstrate those lesions which are due to loss of brain tissue; also many of the congenital cerebral deformations. Even in cases of well defined focal or jacksonian epilepsy, ventriculography often yields most important information prior to a cranial exploration, for many lesions are below the cortex and would escape detection by inspection or palpation of the brain were the ventriculographic evidence not known at the time.

#### THE DIAGNOSIS OF ARTERIOVENOUS ANEURYSM OF THE BRAIN

The signs and symptoms of arteriovenous aneurysms show striking uniformity when taken as a whole. The outstanding complaints are: (1) jacksonian convulsions usually followed by (2) a transient motor or sensory disturbance, and (3) a gradually progressive and permanent motor or sensory paralysis coming on over a period of years and not directly depending on convulsions. When to these are added the long time element, the data are sufficiently characteristic at least to suggest the diagnosis of an arteriovenous aneurysm above other lesions affecting the brain. The transient paralysis following a convulsion and particularly the gradual permanent paralysis (not related to convulsions) makes a tumor formation of some kind an almost certain diagnosis. The accurately repeated jacksonian convulsions, involving such a sharply restricted part of the rolandic area and particularly when covering a period of so many years, should make a true neoplasm very unlikely. When the convulsions begin in early life and extend into the adult life, a neoplasm can almost be excluded. But when the epilepsy begins in later life and the time interval is still short, slowly growing tumors such as the meningiomas are important lesions to be differentiated; likewise they may show pressure symptoms late. Venous angiomas must always enter into consideration. They too will cause transient motor and sensory losses after the jacksonian seizures, but the permanent motor and sensory changes are far less possible, and when they do occur they are less progressive than in the arteriovenous variety. With symptoms, such as

Not infrequently a well defined extracranial arteriovenous aneurysm is demonstrable in patients who also have the intracranial signs and symptoms described for cerebral arteriovenous aneurysms. With such symptoms, an intracranial lesion of the same type is to be expected. An intracranial arteriovenous aneurysm was diagnosed in one of the cases reported here by this method of reasoning (case 6).

#### THE TREATMENT FOR ARTERIOVENOUS ANEURYSMS OF THE BRAIN

Occasionally spontaneous recovery in cases of arteriovenous aneurysm has been reported, but there is little real hope for such a successful outcome either in the brain or elsewhere in the body. The only way to cure an arteriovenous aneurysm is to ligate the entering artery or to excise the vascular tumor. But the radical attempt at cure is attended by such supreme difficulties and is so exceedingly dangerous as to be contraindicated except in certain selected cases. It has never seemed fair to make this attempt except on the insistent demand of the patient who fully understood all phases of the situation. Moreover, there are ways of helping the condition with little if any risk, and this in many cases at least seemed more to be recommended than the attempted extirpation of the vascular mass.

As in most cerebral lesions, however, each case should be considered a law unto itself. There are large aneurysms and small ones; those which are mostly arterial, others mainly venous; some are superficial, others deep; some are in highly important areas of the brain, others in portions largely silent. All of these factors, and finally the patient's wishes in the matter, must be weighed. An aneurysm in the left cerebral hemisphere in a right-handed person is surely *noli me tangere* under all conditions. Any attempted cure, even if successful, would almost surely result in disturbances of speech or motor power, or of both. Aneurysms of the corpus callosal arteries do not offer any greater surgical possibilities.

There is more reason to attempt to cure a patient who has arteriovenous aneurysms in the right cerebral hemisphere. In most of these cases, the arterial connections with the lesions are provided by branches of the middle cerebral artery. Should the aneurysm be postrolandic, the arterial connection can be ligated without injury to the motor function. In one case, we were able to do this without great difficulty. After ligating the arteries supplying the angioma, excision of the vascular bed was easy and relatively bloodless. In another case, in which the anterior pole of the right temporal lobe was covered with great tortuous and distended veins, the anomalous vessel was located and ligated with a silk ligature. It arose from the middle meningeal artery just beyond its origin from the internal carotid; following this the mass of distended

In those cases with the less well defined jacksonian convulsions developing in adult life and without a slow paralysis, one would have little reason to suspect an arteriovenous aneurysm; rather the diagnosis of a cerebral tumor would be considered most probable.

The roentgen-ray evidence, as in one of the cases which I have reported, may, unaided be sufficient for diagnosis. The presence of cal-

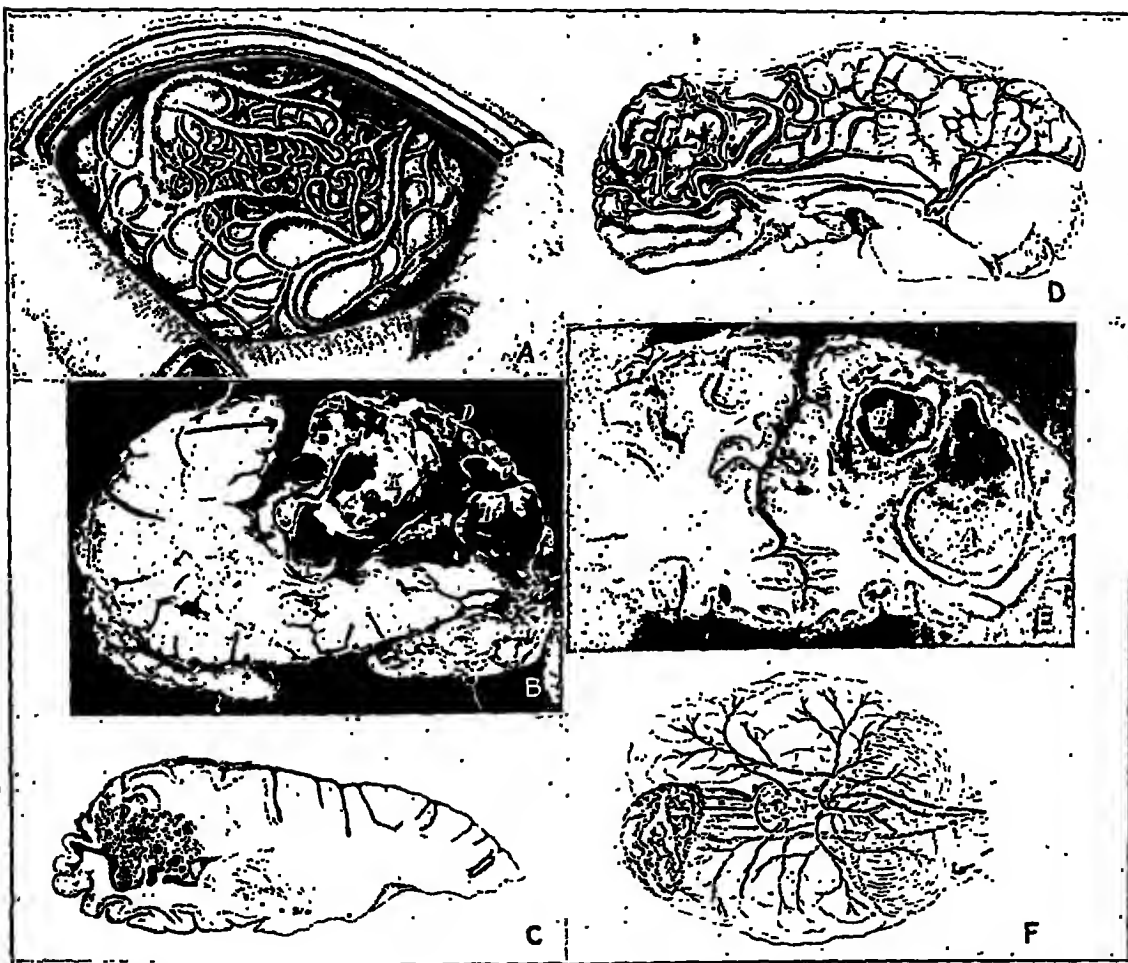


Fig. 32.—Group of specimens from the literature. *A* indicates Campbell and Ballance's case; *B*, Kaiserling's case. The arrow at the top of the brain is directed to the arterial venous connection which Kaiserling has marked *A*; the extensive thrombosis formation is marked *K*. *C* indicates Deetz's case showing the intracranial extension of the aneurysm; *D*, Deetz's case, in which the aneurysm arose from the corpus callosal artery; *E*, Kaiserling's case. This section is anterior to the one in *B*. *F* is taken from Steinheil's case in which the outlet of the aneurysm was into the vein of Galen.

cified shadows in circles or whorls, is, I believe, almost pathognomonic of vascular degeneration. When taken in conjunction with the clinical data, the diagnosis should be unequivocal.

TABLE 2.—Analysis of the Cases of Arteriovenous

Author	Date, Sex, Age	Location	Duration Symptoms	First Symptom	Principal Symptoms	Sign or Symptom of General Pressure	Focal Symptoms	Eye- grounds
Bergmann <sup>42</sup> .....	....	Fossa of Sylvius and paracentral fossa	..	.....	.....	.....	.....	.....
Borchardt <sup>20</sup> .....	1925 ♀ 27	Paracentral	..	.....	Convulsions; paralysis	.....	.....	.....
Campbell and Ballance <sup>14</sup>	1922	Paracentral	..	Weakness of arm and leg; and fits	Mild degree hemiplegia and anesthesia; convulsions	None	Hemiplegia and hemian- esthesia; increased reflexes; ankle clonus	.....
Deetz <sup>20</sup> .....	1902 ♀ 56	Right side of corpus callosum	..	Convulsion	Convulsions; partial hemi- plegia	None	Left hemi- plegia; Jack- sonian con- vulsions	.....
Deist <sup>24</sup> .....	1922 ♂ 56	Paracentral (left)	12 yr.	Convulsion	Convulsions	None	Jacksonian convulsions; Babinski +	Nega- tive
Drysdale <sup>28</sup> .....	1904 ♀ 26	Prerolandic (right)	11 yr.	Convulsion	Convulsions; weakness	.....	.....	.....
Eiselsberg <sup>13</sup> .....	1913 ♂ 39	Paracentral	..	Convulsion	Convulsions; headaches	Headaches	Jacksonian convulsions	.....
Emanuel <sup>22</sup> .....	1898 ♂ 36	Paracentral	30 yr.	Headaches when a boy	Convulsions	Headache; large head	Jacksonian convulsions	.....
Kaiserling <sup>30</sup> .....	1913 ♂ 26	Most of hemi- sphere	..	.....	.....	.....	.....	.....
Kallischer <sup>11</sup> .....	1897 ♂ 7	Sylvian fossa and frontal lobe	1 yr.	Convulsion	Convulsions; hemiplegia grad- ually became complete	None	Convulsions and hemi- plegia	Nega- tive
Krause <sup>8</sup> .....	1908 ♂ 46	Paracentral	..	.....	.....	.....	.....	.....
Laves <sup>25</sup> .....	1925 ♀ 53	Paracentral and post- rolandic	12 yr.	.....	.....	.....	.....	.....
Mühsam <sup>12</sup> .....	1924 ♀ 25	Occipital region	..	.....	Diplopia; headache	Diplopia; headache	.....	Large tortuous vessels; slight choking
Ranzel <sup>36</sup> .....	1909 ♂ 36	Left occipi- tal lobe	2 yr.	Convulsion	Convulsions; some motor and speech disturbance	None	Jacksonian convulsion <sup>4</sup> , hemiplegia, aphasia	.....

venous trunks collapsed. This patient has remained well for three and one-half years; he has had only one convulsion (a year ago), whereas before the fistula was closed, convulsions occurred every month. There is no assurance of a permanent cure of epilepsy even after the cure of an aneurysm. The cerebral defect will always remain at the site of the old lesion and any lesion of the cerebral hemisphere will always remain a potential source of convulsions. However, the convulsions will be far less and more easily controlled with an inactive lesion than with one which is active.

A third and only other attempt at radical cure by extirpation of the angioma was our first experience with a lesion of this type. Thinking at the time that it was a venous angioma, its extirpation after careful ligation of all the superficial veins seemed possible. The huge rolandic vein was doubly ligated and divided both above and below the great mass of cortical vessels and another vein was being sutured when suddenly the rolandic vein burst, not at the site of the sutures, but midway between them. It was then evident that the bleeding was arterial, and that with the venous outlets closed, the arterial pressure within the veins was greater than the wall of the vein would stand. The vein ruptured at the localized swelling shown in the drawing, i. e., at the weakest point and probably where the main force of the artery is projected. This accident demonstrated the danger of closing the veins while the arteries supplying the aneurysm are intact. When the second ligation was being placed on the big rolandic vein it was observed that considerable force was necessary to tighten the knot and occlude the vessel, and it could be done only step by step; the arterial pressure was responsible for this difficulty. Krause's case is interesting in this connection. He, too, ligated some veins on the surface, thinking the angioma to be venous and hoping to benefit the patient by reducing the number of veins. Fortunately nothing happened. He commented on the fact that the ligated veins "ballooned out like sausages." Bergmann's<sup>42</sup> patient died from uncontrollable bleeding; assuming a localized bulge in the dura to be a cyst, a blind puncture into it was followed by terrific bleeding. Laves' patient also was lost on account of hemorrhage following an exploratory puncture of the brain. Once there is a tear in such a nest of vessels, their defective walls almost preclude all chance of controlling the bleeding. Each attempt at hemostasis is promptly followed by more bleeding.

In two of my cases in which the aneurysm was located in the rolandic and prerolandic areas, palliative treatment was tried, the internal carotid artery being ligated in the neck. In one case there have been no attacks.

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42. Bergmann: Zur Kasuistik operativer Hirntumoren. *Arch. f. klin. Chir.* 65:935.



TABLE 2.—Analysis of the Cases of Arteriovenous

Author	Date, Sex, Age	Location	Duration Symptoms	First Symptom	Principal Symptoms	Sign or Symptom of General Pressure	Focal Symptoms	Eye- grounds
Simmonds <sup>14</sup> .....	1905 ♀ 18	Right occipital lobe	6 yr.	Headaches	Headaches, hemiplegia, loss of touch and smell; blindness right eye	Headache	Hemiplegia	.....
Astvazaturoff <sup>15</sup> .	1911 ♀ 35	Right fronto-parietal	..	Convulsion	Convulsions; headache	Headache	Jacksonian convulsions	.....
Simmonds <sup>16</sup> .....	1905 ♂ 55	Right parietal	Since childhood	Convulsion	Convulsions	.....	.....	.....
Steinhell <sup>17</sup> .....	1895 ♂ 49	Right frontal	Since childhood	Convulsion	Convulsions; progressive paralysis and hemianopsia (left homonymous)	.....	Hemiplegia; hemianopsia (left homonymous); Jacksonian convulsions	Normal
Sternberg <sup>18</sup> .....	1905 ♀ 25	Temporal lobe	..	.....	.....	.....	.....	.....
Sterzing <sup>17</sup> .....	1908 ♂ 32	Corpus striatum	22 yr.	Weakness right leg	Hemiplegia; convulsions; some motor aphasia	No	Hemiplegia; Jacksonian convulsions	.....
Struppler <sup>13</sup> .....	1900 ♀ 48	Paracentral	Few hours	Coma	None until coma	No	None	.....
Wichern <sup>11</sup> .....	1912 ♂ 32	.....	..	Hemiplegia	.....	No	Hemiplegia; Jacksonian convulsions	.....
Leunenschloss <sup>27</sup>	1914 ♂ 24	Right cerebellar lobe	15 yr.	Headache	Headache; hemiplegia; deafness; dizziness	Headache	Deafness	.....
Therman <sup>28</sup> .....	1910	Parietal lobe	..	.....	.....	.....	.....	.....
Zaojensky <sup>28</sup> ....	1910	Parietal lobe also cerebellum	..	.....	.....	.....	.....	.....

# Aneurysm Collected from the Literature

Head-ache	General Epilepsy	Focal Epilepsy	How Diagnosed	Diagnosis Before Operation or Autopsy	Operation and Observations	Conditions at Necropsy	Remarks
..	..	..	Operation and necropsy	Brain tumor	Large veins on surface of brain	Walnut sized knot of vessels beneath surface of brain, very tortuous	Puncture of dura blindly; terrific hemorrhage, uncontrollable, death; diagnosed cavernous angioma
..	+ right	..	.....	.....	.....	Section shows aneurysm	Old specimen from Virchow Krankenhaus; patient died in childbirth of cerebral hemorrhage
After attacks	..	+ left toes	Operation	Tumor	Large veins on surface	Living .....	Hemiplegia and hemianesthesia were gradually progressive
..	..	+ left-sided	Necropsy	.....	.....	Right corpus callosal artery large and tortuous; mass of vessels plunged into frontal lobe	Very extensive tumor covers mesial surface of hemisphere, fills frontal lobe and reaches anterior horn of ventricle and corpus striatum
None	..	+ right leg	Necropsy	.....	.....	Large veins on surface	
..	..	+ arm and leg	Necropsy	.....	.....	Anterior cerebral artery very large; hemorrhage	Large veins on surface obscured brain; patient gradually became more and more deeply comatose following fit 10 days previously
+	..	+ right side	Operation	.....	Large veins on surface	.....	Very large veins on surface of brain; ligated; condition of patient unchanged
In youth only	..	+ arm	Necropsy	.....	.....	Large surface veins; mass of vessels in brain grown into ventricle and choroid plexus, also extended to pulmonary	Patient died in coma following attack; was excused from military duty because of headache; vessels are thrombosed and calcified; no mention of cerebral hemorrhage
..	..	+	Necropsy	.....	.....	Large surface veins	No history, except that patient died in coma following attack; this is a remarkable specimen, the veins and arteries being sharply defined; the communication is shown in the photograph; the venous channels are larger than in any other case; there is no network of vessels
None	..	+ right corner of mouth	Necropsy	.....	.....	Large veins on surface and mass of vessels in frontal lobe	No change in big arteries at base of brain; Virchow said it was an unusual case
..	..	+	Operation	.....	Ligated some veins, says they then distended like sausages	Large surface veins; smaller vessels of the tumor just reach the surface	Typical surface appearance of lesion shown in painting
..	..	+ left hand	Operation and autopsy	.....	Large veins on surface; no thrill or pulsation	Cluster of entwined vessels below surface	No loss of consciousness in earlier attacks; at operation brain was punctured, severe bleeding which was uncontrollable; branch of middle cerebral artery (containing small accumulated aneurysm) enters vascular tumor which protrudes into ventricle; hypertrophy of heart
+	..	..	Necropsy	.....	.....	.....	A pulsating tumor near lision connects with veins of brain and longitudinal sinus; also pulsating exophthalmos; very large veins in dura and in the brain seen on its surface
..	..	+ right arm	Necropsy	.....	.....	Small knot of vessels in left occipital lobe	Patient died of hemorrhage in an attack

either petit or grand mal, since the operation (two and one-half years). The other patient, roentgenograms of whom showed the extensive calcification, was free from attacks for a year, after which they gradually recurred with practically the same intensity and frequency as before operation. The latter patient being 47 years old, the carotid was at first only partially ligated with a band of rubber tissue. Three weeks later, it was found to be totally occluded by a thrombus.

A subtemporal decompression and excision of the extracranial aneurysm (of the scalp) were performed in another patient who was losing vision because of a long-standing papilledema. His headache was relieved, but his condition otherwise was unchanged.

The cerebellar arteriovenous aneurysm had caused hydrocephalus. This was relieved by the bilateral cerebellar decompression which, as a routine, remains after a cerebellar exploration. The decompression remained full and tight until it was later relieved by ligation of the left vertebral artery in the neck. At operation, the intracranial portion of this artery was found to be several times its natural size, and this led to the belief that it supplied the arterial connection to the aneurysm. When exposed between the atlas and occipital bone, this great tortuous artery was just as large as the intracranial portion. Following its ligation, the bulging decompression subsided and has remained in this condition. Although his neurologic symptoms have greatly improved or disappeared, the mental disturbance still persists.

Ligation of the vessels, whether internal carotid or vertebral, can hardly result in a cure. Only an amelioration of the signs and symptoms can be expected, and doubtless even this cannot be permanent. The precedent for such ligations is the treatment of arteriovenous aneurysms between the carotid artery and the cavernous sinus. Following ligation of the internal carotid for these traumatic aneurysms, there is much improvement but usually not a cure. The collateral supply through the circle of Willis militates against a cure; it is fair to presume the same free collateral circulation will preclude the cure of the intracranial aneurysms.

#### SUMMARY AND CONCLUSIONS

1. Eight arteriovenous aneurysms of the brain are presented from a series of tumors of the brain. Twenty-two additional cases have been assembled from the literature.

2. Arteriovenous aneurysms of the brain are similar to those of the vascular system elsewhere in the body, except that traumatic arteriovenous aneurysms probably do not occur in the brain, because large arterial and venous trunks are not in apposition.

3. There are two other types of arteriovenous aneurysms, one in which an anomalous vessel of congenital origin establishes a direct end

*Aneurysms Collected from the Literature—Continued*

Head-ache	General Epilepsy	Focal Epilepsy	How Diagnosed	Diagnosis Before Operation or Autopsy	Operation and Observations	Conditions at Necropsy	Remarks
+	None	None	Necropsy	.....	.....	Enormous dilated veins on surface; tumor of entwined blood channels	There was much thrombosis with some evidence of cannalization; patient died of cerebral hemorrhage from attack
+	..	+ left side	Necropsy	.....	.....	Mass of vessels size of dove's egg below cortex right frontoparietal region; enlarged veins on surface of brain	Patient died of meningitis; calcareous deposits in vessels of vascular mass
..	..	..	Necropsy	.....	.....	Specimen shows a large coiled vessel with many pouching dilatations; no note about veins	It is open to question whether this case is an arteriovenous aneurysm; patient died of cerebral hemorrhage (into ventricle)
..	..	+ left face	.....	Epilepsy; later, aneurysm	.....	Left corpus callosum artery large and tortuous; right vena galeni parva and vena galeni magna large; tumor consists of mass of entwined vessels	Patient finally became demented; vessels of tumor did not seem either like normal veins or arteries; they were large cavernous spaces
..	..	..	Necropsy	.....	.....	Mass of blood vessels in brain	Drawing of vessels suggests arteriovenous aneurysm
..	..	+ right	Necropsy	.....	.....	Mass of vessels deep in corpus striatum; extends into ventricle at caudate nucleus; connection with choroid plexus vessels	When 10 years old patient suddenly developed weakness of right arm and leg; then improved and became stationary for 20 years when paralyzed anew; 11½ years later coma and death from cerebral hemorrhage
None	None	None	Necropsy	.....	.....	Mass of small vessels in Rolandic area	Patient died of cerebral hemorrhage; this lesion may or may not be an arteriovenous aneurysm; it has been described as a cavernous angioma
..	..	+ right side	.....	.....	.....	Hemorrhage into ventricle and subarachnoid space; tumor of vessels 6 by 3 cm. in frontal region	When 10 years old hemiplegia suddenly developed on the right side with speech disturbance; gradual return of function and stationary condition for 21 years when paralysis and later convulsions developed
+ localized in back	No	No	Necropsy	.....	.....	Vascular bed of vessels in right cerebellar lobe, anterior and posterior inferior cerebellar arteries run into angioma	Death from hemorrhage; much calcification and thrombosis in vessels
..	..	..	Necropsy	.....	.....	Large surface veins; collection of vessels in parietal lobe projects into ventricle	Accidental finding at necropsy following operation for sarcoma of jaw; extensive thrombosis of cortical veins even of longitudinal sinuses; dilated venous trunks are localized to region draining angioma
..	..	..	Necropsy	.....	.....	.....	This article is written in the Russian language but apparently there are two independent intracranial arteriovenous aneurysms; photographs appear to establish the lesion as arteriovenous

# LIGATION OF ARTERY AND CONCOMITANT VEIN IN OPERATIONS ON THE LARGE BLOOD VESSELS\*

FRANK V. THEIS, M.D.

Resident Surgeon of the Presbyterian Hospital of Chicago

CHICAGO.

The beneficial effect of occluding the satellite vein when ligation of the artery becomes necessary in surgical conditions of the large blood vessels was first recognized by Sir Arthur Makins<sup>1</sup> in 1913. He found a lessened incidence of gangrene in following this procedure. Nevertheless, during the early part of the World War, careful preservation of the vein was practiced, but the occurrence of gangrene following ligation of the large artery to the extremity brought forth interesting and valuable investigations on the subject. Drummond<sup>2</sup> showed experimentally that ligation of both artery and vein produced "little or no change" in the condition of the loops of cat's intestines. When the artery alone was occluded, definite gangrene of the segment usually appeared within twenty-four hours. Van Kend<sup>3</sup> attributed the decreased frequency of gangrene to a "slight rise in the blood pressure in the limb following application of a ligature to a vein, after previous ligature of the artery." He demonstrated this rise in blood pressure with plethysmographic tracings. With these and other reports presented at the Inter-Allied Conference of Surgeons in Paris, in May, 1917,<sup>4</sup> the conclusion was reached that "facts tend to prove, even when the wound is limited to the artery, that simultaneous occlusion of the unwounded vein is to be recommended." The subsequent application of this procedure in the surgical treatment of arteriovenous aneurysms still further strengthens its clinical advantages.<sup>5</sup>

Application of the principle of ligation of the vein in cases of spontaneous gangrene seems to be gaining increased favor as evidenced by its more frequent mention in the surgical literature. In most of these

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\* From the Surgical Department of the Presbyterian Hospital and Rush Medical College of the University of Chicago.

1. Makins, Sir Arthur: *Gunshot Injuries to the Blood Vessels*, New York, William Woods & Company, 1919.

2. Drummond, Hamilton, quoted by Halsted: *Johns Hopkins Hosp. Rep.* 21: 1, 1921; quoted by Makins (footnote 1).

3. Van Kend, M., quoted by Makins (footnote 1).

4. *Compt. rend. Conf. Chir. Interall., Paris*, 1917.

5. Halsted, W. S., *Johns Hopkins Hosp. Rep.* 21:1, 1921. Holman, Emil: *Ann. Surg.* 85:173 (Feb.) 1927.

to end communication between an artery and vein; the other in which a network of vessels—a so-called angioma—is interposed between an artery and one or several veins. A capillary bed between the artery and vein is lacking in both types; the arterial blood, therefore, passes directly into the veins.

4. Both types are evident by the large, full and tortuous veins on the surface of the brain. A thrill can usually be felt, and red arterial blood can be seen pumping into the dark venous blood. The observations make the diagnosis absolute. There are usually congenital abnormalities of the surface veins of the brain.

5. Arteriovenous aneurysms of the brain are not uncommon, occurring in about 1 per cent of a series of tumors of the brain. They are located in almost every part of the brain.

6. The symptoms are fairly uniform and characteristic. Jacksonian convulsions, followed by transient loss of sensation or motor power in the part affected by the convulsion, and a gradually progressive sensory or motor hemiplegia on the affected side, are the symptoms common to most of the aneurysms affecting the cerebral hemispheres. The symptoms are usually of many years' duration, often beginning in childhood and continuing into adult life; again, they frequently do not begin until after the thirtieth or fortieth year.

7. General pressure symptoms, like those of a tumor of the brain, do occur, but in a minority of cases.

8. Cerebral hemorrhages occurred in about 40 per cent of the cases. It is the principal cause of death.

9. Changes shown by the roentgen ray are at times helpful in making a diagnosis and occasionally are pathognomic. Ventriculography helps to determine the existence of a space-occupying lesion.

10. The treatment is of two types: (1) ligation of the entering arteries, with or without extirpation of the mass of vessels—so-called angioma; (2) ligation of the internal carotid artery (for cerebral aneurysm) or of the vertebral artery (for cerebellar aneurysm). Occasionally, a subtemporal or cerebellar decompression (depending on the location of the aneurysm) may be indicated.

Radical ligations or extirpations alone are curative, but are exceedingly dangerous to life and function and indicated in the minority of cases, when the aneurysm is posterior to the motor tracts.

With these conflicting reports in mind, two methods were used to study the collateral circulatory bed which develops when the main arterial supply of the limb is interfered with.

1. Roentgen-ray visualization of the vascular bed in:
  - (a) Amputated lower extremities in which the vessels were pathologic.
  - (b) The study of the lower limbs of experimental animals following ligation of the artery alone on the one side as compared to the ligation of the artery and vein on the other side. This study was made on different animals over various periods of time up to three months after the operations.
  - (c) The effect on the visualization of the collateral circulation by varying the pressure of the injection of the opaque emulsion into the diseased vessels of the amputated limbs on the one hand, and the normal vessels of the animals, on the other.
2. Determinations of the volume of blood flow were made over various periods of time on the surviving experimental animal. The determinations were made from the distal open end of the ligated femoral artery below the profunda with and without simultaneous ligation of the vein.

#### ROENTGEN-RAY VISUALIZATION OF THE CIRCULATORY BED

*Blood Vessels in Amputated Legs.*—Roentgen-ray visualization of the circulatory bed was first used by Drummond<sup>2</sup> in his original work on ligation of the arteries and the veins. Meleney and Miller,<sup>14</sup> in studying the collateral vascularity in amputated limbs for gangrene, were the first to publish its value, in a most comprehensive article. Lewis and Reichert<sup>15</sup> also published a similar investigation with the use of bismuth oxychloride and acacia emulsion as the material for injection instead of the previously used barium. In my experiments I find that the bismuth emulsion as recommended by Hill<sup>16</sup> gives the most perfect roentgenograms of the arterial tree and collaterals without diffusing into the surrounding tissues as is seen when sodium iodide solution is used. On the other hand, barium does not throw so dense a shadow as metallic mercury, and both of these are too coarse to fill the finer arterioles.

The outstanding roentgenograms of ten amputated limbs that I have studied are taken in two cases of thrombo-angiitis obliterans. The clinical histories in both cases were almost identical. In the one case, the patient was 50 years of age and of German descent. He had had symptoms of intermittent claudication, pain in the calf of the leg and discoloration and numbness of the right foot almost continuously for five years. The other patient was 48 years of age, a Russian Jew who had had similar symptoms for only two years. In both there was a complete absence of pulsation in the dorsalis pedis, posterior tibial and popliteal arteries. Even the results of the intracuticular salt solution

14. Meleney and Miller (footnote 9, sixth reference).

15. Lewis and Reichert (footnote 9, seventh reference).

16. Hill (footnote 9, eighth reference).

cases, however, there has been a previous gradual occlusion of the main artery to the extremity. In 1913, Oppel<sup>6</sup> was the first to report improvement following ligation of the popliteal vein in six cases of threatened senile gangrene of the foot. He attributed the encouraging results to the retardation of the venous return flow and the consequent rise in the blood pressure of the limb. Stradin<sup>7</sup> also employed ligation of the vein in cases of spontaneous gangrene, reporting good results, but he combined it with sympathectomy. McWhorter<sup>8</sup> recently presented before his clinic at the Presbyterian Hospital, three cases of thrombo-angiitis obliterans with ligation of the femoral vein. Two of the patients had subsequent amputations, although the third showed encouraging improvement over a period of five months. As a result of experiments on animals, Brooks,<sup>9</sup> Holman<sup>10</sup> and Pease<sup>11</sup> have corroborative evidence for employing simultaneous ligation of the vein when the artery is occluded.

In reviewing the literature, however, I found that the final results of McNealy,<sup>12</sup> Thurston<sup>13</sup> and others, who employed ligation of the femoral vein in cases of spontaneous gangrene, were discouraging. While the value of occluding the venous return flow may not be overestimated when sudden obstruction of the artery occurs, its further use in conditions of chronic occluding diseased processes in the arteries is of doubtful value.

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6. Oppel: *Zentralbl. f. Chir.* **31**:1241, 1913.

7. Stradin, P.: *Deutsche Ztschr. f. Chir.* **194**:289 (Jan.) 1926.

8. McWhorter, Golder, L.: Personal observation and communication.

9. Brooks, Barney, and Martin, Kirley: Simultaneous Ligation of the Vein and Artery, *J. A. M. A.* **80**:1678 (June 9) 1923. Holman, Emil and Edwards, Muriel, New Principle in Surgery of Large Vessel; Ligation of Vein Proximal to Site of Ligation of Artery, *J. A. M. A.* **80**:909 (March 19) 1927. Pease, Herman: *Ann. Surg.* **86**:850 (Dec.) 1927. McNealy: *Surg. Gynec. Obst.* **40**:45 (Jan.) 1925. Thurston, J. A.: *Bull. U. S. Vet. Bur. Med.* **1**:1 (Dec.) 1925. Meleney and Miller: *Ann. Surg.* **81**:976, 1925. Lewis and Reichert: Collateral Circulation in Thrombo-Angiitis Obliterans; Indication for Ligation of Femoral Artery First Distal to Profunda, *J. A. M. A.* **87**:302 (July 31) 1926. Hill, E. E.: *Bull. Johns Hopkins Hosp.* **35**:318, 1924. Halstead (footnote 5, first reference). Holman (footnote 5, second reference). Sehrt, E.: *Med klin.* **12**:1338, 1916. Stern and Cohen: Intracutaneous Salt Solution Wheal Test; Its Value in Disturbances of Circulation in Extremities, *J. A. M. A.* **87**:1355 (Oct. 23) 1926. Brooks and Jostes: Clinical Study of Diseases of the Circulation of the Extremities: Description of a New Method of Examination, *Arch. Surg.* **9**:485 (Nov.) 1924.

10. Holman (footnote 9, second reference).

11. Pease (footnote 9, third reference).

12. McNealy (footnote 9, fourth reference).

13. Thurston (footnote 9, fifth reference).



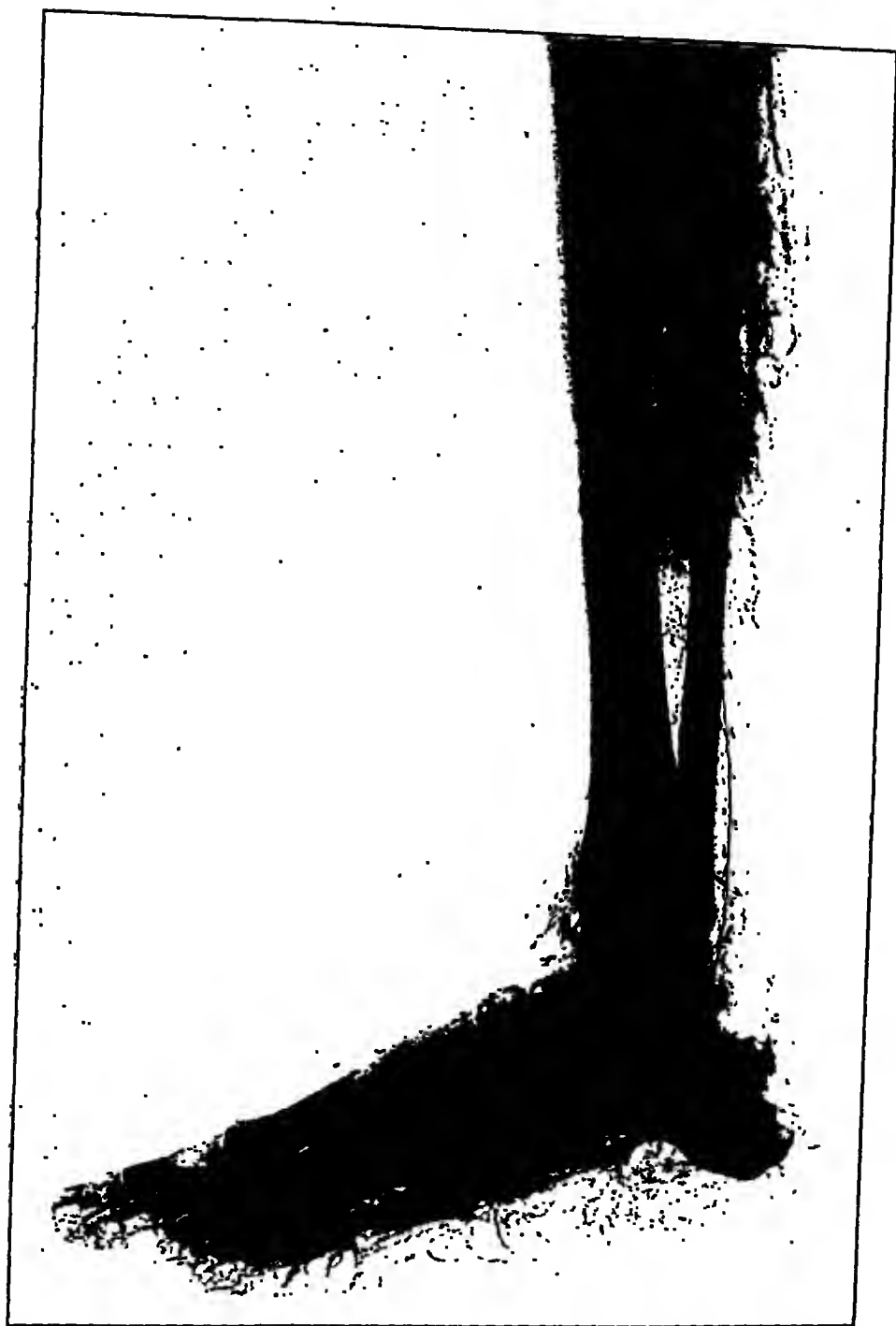


Fig. 1.—Roentgen-ray visualization of the vascular bed in leg amputated for thrombo-angiitis obliterans. Note the extensive collateral vascular bed with almost complete occlusion of the main arteries.

test<sup>17</sup> were exactly similar, indicating the same degree of apparent circulatory deficiency—the wheals disappearing within from five seconds on the great toe to one hour plus on the thigh. In the first case, amputation was performed because of rapidly spreading gangrene with infection; in the second, because of the extreme unremitting pain in the calf of the leg, but no gangrene. Microscopic and macroscopic examination of the arteries confirmed the diagnosis and showed almost the same degree of involvement. After injection of the popliteal artery in each case, roentgen-ray visualization revealed an extensive collateral vascular bed to account for the absence of gangrene in the one case (fig. 1), while in the other, with a much longer duration of the symptoms, an almost complete absence of the collateral vessels was found. This suggested the probability that there might be some controllable factors which could increase the formation of collateral vessels in cases of this kind.

*Vascular Bed in Experimental Animals After Ligation of the Superficial Femoral Artery, With and Without Simultaneous Occlusion of the Common Iliac Vein.*—Ten experiments on animal were carried out to determine the effect on the collateral circulatory bed of ligating the proximal satellite vein with the artery as compared to the ligation of the artery alone. The superficial femoral artery was ligated just below the profunda femoris on both sides, but in addition, the common iliac vein was simultaneously ligated on the right side. The animals were killed at various periods, from immediately after to three months after operation. The abdominal aorta was then injected with the bismuth oxychloride emulsion under a pressure of 125 mm. of mercury. Roentgen-ray visualization immediately after the operation showed the collateral vascular bed to be best where both the artery and the vein were ligated (fig. 2). In three weeks, however, the vascular bed was more developed where the artery alone was occluded, as compared to the opposite side where the common iliac vein was occluded simultaneously with the artery (figs. 3 and 4).

*Vascular Bed During Variation in the Pressure of the Injections.* The much discussed influence of elevating the blood pressure in certain cases of circulatory deficiency due to peripheral arterial disease suggested the study of the vascular bed with variation in the pressure of injection of the extremities. Amputated limbs were first injected with a manometer pressure of around 150 mm. of mercury, the patient's own blood pressure (fig. 5). Roentgenograms were then taken and the limbs reinjected with double the pressure (300 mm. of mercury) (fig. 6). Only the faintest improvement in the finer arterioles could be detected even with such a marked increase in pressure. Further increase of pressure, however, improved the bed considerably. This probably

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17. Stern and Cohen (footnote 9, ninth reference).

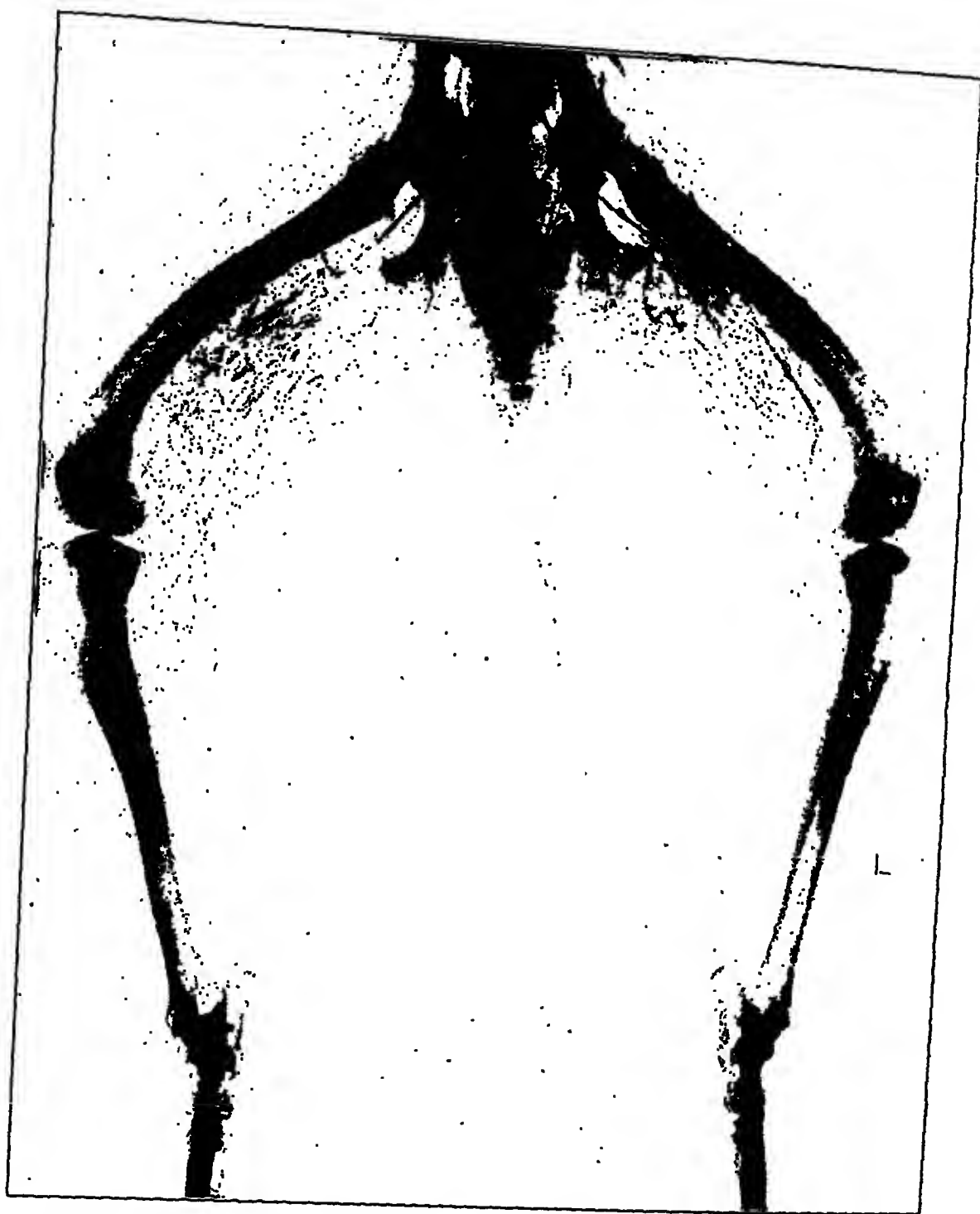


Fig. 3.—The vascular bed of the lower extremities of an animal three weeks after operation shows equal development on both sides. On the right leg the artery and vein were simultaneously occluded while on the left only the femoral artery was ligated. Note the large obturator arteries which are now the main source of arterial supply to the extremities.



Fig. 2.—Roentgen-ray visualization with injection of the abdominal aorta under a pressure of 125 mm. of mercury immediately after operation. The collateral vascular bed is seen to be more developed where the artery and concomitant vein have been simultaneously ligated (left side of picture).

accounts for some of the excellent roentgenograms that are frequently seen when an accurate check is not made to determine the pressure back of the injection. In order to eliminate the postmortem changes as much as possible, the limbs were studied immediately after amputation.

Considering the slight rise in blood pressure and the clinical advantage of simultaneous ligation of the satellite vein with the artery, the effect of moderate variations in the pressure of the injected material on the normal vessels of experimental animals was next studied. In order to bring out the collateral vascular bed of the nonpathologic arterial tree, the superficial femoral artery on both sides was occluded. The animal was killed, and the abdominal aorta was injected with the opaque mass under a pressure of 100 mm. and 150 mm. of mercury, and roentgenograms were made after each injection. In contrast to the slight improvement seen when the vessels were pathologic, the normal vessels showed marked improvement of the collateral bed when the pressure of the injection was increased. No doubt this difference was due to the fact that the elasticity of the artery is lost in the diseased vessel.

*Determinations of the Volume of Blood Flow With and Without Ligation of the Concomitant Vein.*—The temporary immediate improvement of the collateral circulatory bed with concomitant ligation of the vein as was seen in the roentgen-ray visualizations suggested the advisability of determining the volume of blood flow over a period of weeks in surviving experimental animals. This was next studied on dogs at twenty operations.

#### EXPERIMENTAL WORK

Large male dogs were used. Under a light ether anesthesia, the right superficial femoral artery was isolated. After a temporary distal ligature was applied, a citrated 18 gage transfusion cannula was inserted proximally into the artery. The normal flow averaged about 240 cc. per minute. The flow in each case was obtained for from five to ten seconds, and the minute determination calculated therefrom. When the cannula was removed a ligature was applied proximal to the opening in the artery, and the cannula was reinserted distally. Through an incision over the lower right rectus muscle, a previously introduced ligature around the common iliac vein was tied. The immediate flow per minute from the distal end of the ligated artery was 48 cc.; in ten minutes it was the same, in thirty minutes, 51 cc., and in one hour, 54 cc. Three weeks later, the same procedure was followed on the left femoral artery, but without occlusion of the common iliac vein. The normal proximal flow was found to be the same as on the right side. From the distal end of the ligated artery, the flow immediately following the ligation was 39 cc., increasing to 42 cc. in ten minutes, 48 cc. in thirty minutes, and 54 cc. in one hour. At the same operation, the distal end of the ligated right femoral artery of the previous operation was again isolated and cannulized. The flow was found to be 96 cc. per minute, having increased from 54 cc. during the three week interval. The distal end of the left femoral artery was recannulized at a subsequent operation three weeks later, and was found to have increased from 54 to 136 cc. per minute. All the factors, including the depth of the ether anesthesia were kept as constant as possible. No more than 50 cc. of blood was withdrawn at one operation.



Fig. 4.—Six weeks after operation the vascular bed shows greater development on the left leg where the artery alone has been ligated as compared to the right side with both artery and vein occluded.

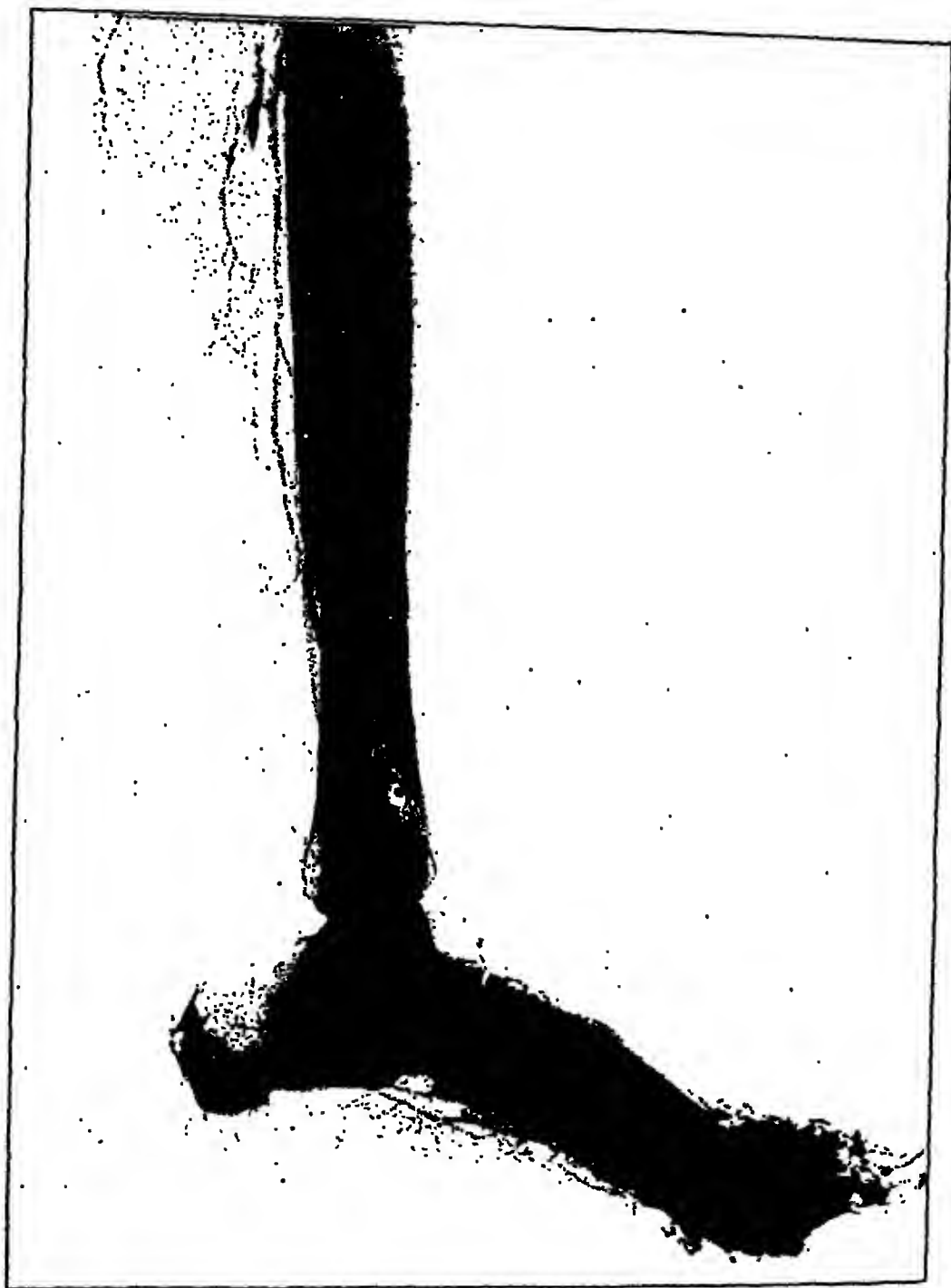


Fig. 6.—Same limb as in figure 5 with reinjection under a pressure of 300 mm. of mercury. Note that even with double the pressure only the faintest improvement in the collateral vascular bed can be detected.

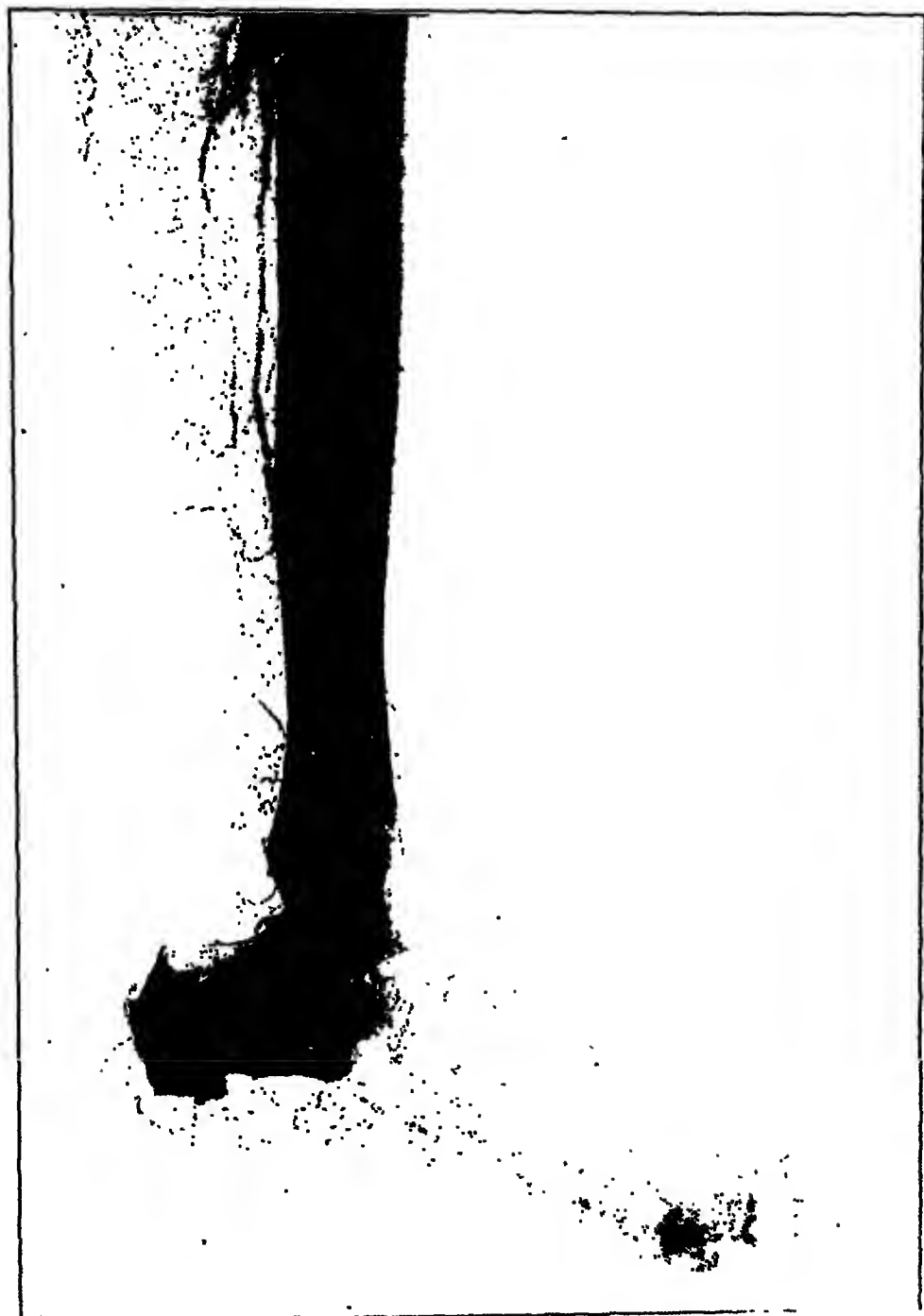


Fig. 5.—Amputated limb with the injection of the opaque mass under a pressure of 150 mm. of mercury.



*Results.*—Immediate transitory increase in flow from the distal end of the ligated femoral artery was obtained where the proximal concomitant vein was simultaneously occluded.

In the experiments in which the artery alone was ligated, this temporary increase was overcome and exceeded within one hour in all the animals. Moreover, when the artery alone was ligated, in one of the animals the normal flow as previously determined from the proximal end of the ligated artery returned within six weeks (fig. 7).

*Determination of Blood Volume Flow in Cubic Centimeters on Dogs \**

Dog	Normal	Immed. Oc.	Minutes					Weeks			
			10	20	30	40	60	2	3	4	6
I	R—	30	..	..	..	..	..	..	..	..	..
	L—	25	..	..	..	..	..	..	..	..	..
II	R—	20	..	..	..	..	..	..	..	..	..
	L—	20	..	..	..	..	..	..	..	..	..
III	R—	10	..	..	..	..	..	..	..	..	..
	L—	14	..	..	..	..	..	..	..	..	..
IV	R—	10	..	..	..	..	..	..	..	..	..
	L—	9	..	..	..	..	..	..	..	..	..
V	R—	15	..	..	..	..	..	..	..	..	..
	L—	12	..	..	..	..	..	..	..	..	..
VI	R—	14	..	..	..	..	..	..	..	..	..
	L—	12	..	..	..	..	..	..	..	..	..
VII	R—	32	..	..	..	..	..	..	..	..	..
	L—	32	..	..	..	..	..	..	..	..	..
VIII	R—	12	..	..	..	..	..	..	21	..	..
	L—	12	..	..	..	..	..	..	48	..	..
IX	R—	14	..	..	..	..	..	32	..	..	..
	L—	11	..	..	..	..	..	42	..	..	..
X	R—	22	..	..	..	..	..	..	..	..	52
	L—	20	..	..	..	..	..	..	..	..	63
XI	R—220	16	..	..	..	..	..	..	..	..	..
	L—220	12	..	..	..	..	..	..	..	..	..
XII	R—190	48	48	..	48	..	..	..	..	60	..
	L—220	42	42	..	..	54	60	..	..	90	..
XIII	R—264	80	80	90	90	..	..	..	..	..	?
	L—240	72	48	51	54	..	..	..	..	..	210
XIV	R—240	13	18	..	24	..	24	..	..	..	36
	L—240	15	18	..	21	..	24	..	..	..	42
XV	R—240	48	48	..	51	..	54	..	..	96	..
	L—252	39	42	..	48	..	54	..	..	130	..

\* The left superficial femoral artery was ligated alone while on the right side the common iliac vein was simultaneously ligated with the artery. The normal flow was obtained by cannulizing the proximal end of the ligated artery, and the other determinations were made from the distal end. The flow was obtained for from five to ten seconds and the minute volume determinations calculated from the amounts obtained.

Pulsation in the distal part of the artery returned somewhat more slowly but to a final greater volume when the vein was left patent. This is in accord with the determinations of the blood flow shown in the table.

Atrophy, disability or gangrene did not develop following ligation of the superficial femoral artery, irrespective of the patency of the vein. In most cases, the circulation was decreased to below 10 per cent of normal.

#### COMMENT

The slight increase in the residuary arterial pressure after ligation of the artery and concomitant vein, as found by Van Kend, Brooks, Holman and Pease, must be a deciding factor in the immediate transitory improvement in the blood flow when the blood vessels are normal.



Fig. 7.—The left superficial femoral artery was ligated alone. After previous determination of the normal volume flow from the proximal end of the artery, six weeks later at subsequent operation, exactly the same flow was obtained distal to the ligation. Note in the roentgen-ray visualization the extensive development of the collateral bed which practically equals that on the right side where the circulation had not been disturbed!

With the gradual occlusion of the arterial tree that has already taken place in cases of threatened gangrene of the extremities from arterial disease, less benefit would be derived from the initial improvement following proximal ligation of the satellite vein. In these cases, the collateral vessels have had an opportunity to develop during the time that the main artery had become occluded. It is then probable that the ordinary course of events are insufficient to open the potential collaterals. The principle of ligation of a proximal satellite vein is neither applicable nor warranted as a surgical procedure in cases of spontaneous gangrene resulting from arteriosclerosis or thrombo-angiitis obliterans.

When the final maximum increase in the collateral vascular bed rather than immediate improvement is necessary, as in cases of thrombo-angiitis obliterans and other forms of threatened gangrene, ligation of the artery alone is to be recommended. Both on experimental grounds and clinically, as advocated by Lewis and Reichert,<sup>15</sup> this procedure is most likely to give the best results.

#### CONCLUSIONS

The results of the determinations of the volume of flow and the study of the injected collateral vascular bed in experimental animals show that the final increase in collateral vessels is far better when the vein is patent.

With sudden occlusion of a large artery, as in embolism or injury to the vessel, the immediate improvement in the collateral bed due to ligation of the concomitant vein is needed to maintain the vitality of the limb.

When a certain amount of collateral vessels have had an opportunity to develop, as in threatened spontaneous gangrene, surgical procedures on the main vessels of the extremities should be limited to the artery alone.

Contrary to the results reported by Holman, Brooks and others, my experiments show that the increased volume of flow with the artery and the proximal main vein ligated is only slight and transitory. After the initial improvement, there is a retardation of the volume of flow in the subsequent determinations as compared to the increase occurring on the side where the artery alone is occluded.

During the World War, ligation of the artery alone for aneurysm of the femoral artery in surgical procedures was followed by gangrene in more than 50 per cent of the cases. In experiments on dogs and rabbits, Brooks<sup>18</sup> reported the occurrence of gangrene in 71.5 per cent of the animals in which the artery alone was occluded and in 33.3 per cent in which both the artery and the satellite vein were ligated. In both instances, the femoral artery was ligated at the same level. Schrt<sup>19</sup> reported 20 and 9 per cent of gangrene respectively, with ligation of the femoral artery, and with simultaneous ligation of the femoral artery and vein. Irrespective of the site of the occlusion of the femoral artery, gangrene occurred less frequently when both artery and vein were occluded. Clinically, one sees gangrene develop following embolism of the popliteal artery, but not necessarily when the arterial occlusion is more gradual as in many cases of arteriosclerosis and thrombo-angiitis obliterans. Although in my series of experiments on dog, atrophy or gangrene failed to develop with occlusion of the superficial femoral artery below the profunda with or without simultaneous ligation of the common iliac vein, the ability of the collateral vascular bed to develop sufficiently rapidly is of more importance as a cause of gangrene than the point of occlusion of the artery.

The practice of ligation of the artery and the concomitant vein in traumatic surgical procedures, especially in the treatment of patients with arteriovenous aneurysm, is recognized to be of great clinical value. Experimentally, it has been impossible to confirm the enormous improvement with ligation of the artery and the proximal vein as found by Holman.<sup>10</sup> The difference in the results may be due to the fact that his work was done on rabbits over a short period of time and with the use of a noncoagulant in the blood. However, roentgen-ray visualization soon after the operation showed the most marked development of the vascular bed where the vein had been simultaneously occluded (fig. 2). Singularly enough, this immediate temporary benefit following simultaneous occlusion of the satellite vein in cases of sudden arterial obstruction may be the deciding factor in maintaining the vitality of the limb, the absence of which predisposes to the frequent occurrence of gangrene.

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18. Brooks (footnote 9, first reference).

19. Schrt (footnote 9, tenth reference).

are multiple in both kidneys, and the symptoms and shape of the stones warrant surgical intervention, every effort should be made to preserve renal tissue.

The patient's age may also be a factor in determining the operative procedure. In a case of unilateral multiple stones in an old person nephrectomy may be advisable, whereas a similar condition in a young person might warrant conservative operation. If a patient more than 60 years of age has a renal stone that is causing few or no symptoms, the stone may be left; if the patient were younger, removal would be indicated.

#### DIFFERENTIAL RENAL FUNCTION

The comparative estimation of function of either kidney by present methods is notoriously uncertain and misleading. Because of reflex irritation caused by the presence of stone in the renal tissue, the tests of function are frequently inaccurate. It has been our experience that reliance can be placed only on high and low values. The normal or nearly normal return of dye from the affected kidney can be accepted as an accurate index of the condition. No return of dye, or only a trace, usually indicates marked destruction of renal tissue, although in some cases a surprising amount of good renal tissue is found at operation. Intermediate values of dye return are inaccurate, and little reliance can be placed on their interpretation.

Intravenous injection with indigo carmine is the simplest functional method. The intensity of the color of the urine from either ureteral orifice affords a rough but fair index of the renal function. The differential phenolsulphonphthalein test is usually more accurate in determining the degree of reduction in function, but is equally subject to reflex inhibition of secretion and to technical error because of leakage around the ureteral catheter and faulty drainage. Nevertheless, in determining the type of operation in cases of multiple stones, especially of bilateral nephrolithiasis, differential renal functional tests may be of decisive practical value. Pyelography may be more accurate in giving an estimate of renal function than any dye test by outlining the extent and character of the pyelectasis or other deformity. In other words, extensive destruction of renal tissue is rare when the pyelogram demonstrates a comparatively normal pelvis. However, if there is evidence of marked pyelectasis, elongation and dilatation of all calices, cortical necrosis, cicatricial changes, or marked atrophy of the renal pelvis, renal injury is usually considerable, and nephrectomy may often be desirable.

#### RENAL FLUOROSCOPY

There is no preoperative diagnostic method which will always enable one to determine the exact number of stones present, even though shadows visible in the roentgenogram may be identified as intrarenal.

# MULTIPLE RENAL STONES

PROBLEMS IN THE TREATMENT OF PATIENTS WITH THIS CONDITION

WILLIAM F. BRAASCH, M.D.

AND

JOHN L. CULLIGAN, M.D.

Fellow in Urology, The Mayo Foundation

ROCHESTER, MINN.

The indications for operation in the presence of multiple stones in the kidney are not standardized and are influenced largely by the clinical data in the individual case. The tendency in recent years has been toward conservation. If in the complete removal of stones the kidney is not too greatly injured, and if it is shown that considerable function remains, the kidney should be saved. It may be comparatively easy to remove the kidney, but it requires experience and the cooperation of several technical aids to remove all the stones successfully and save the kidney. Among the factors which must be considered in determining the advisability of conservative operation are the size, shape and number of stones, the area involved, the function of the organ and the age of the patient.

## SIZE AND SHAPE OF STONES

It should be recognized that the removal of large branched stones may necessitate considerable destruction of renal tissue. The removal of round, smooth stones, even if they are of considerable size, causes much less injury than removal of branched or coraliform stones which fill the pelvis and calices. Round stones are usually situated in the pelvis and seldom involve the calices; therefore their removal by pelvicolithotomy is usually comparatively easy. If a branched stone involves but one calix, destruction of renal tissue resulting from its removal is not extensive. When, however, all the calices are involved, complete removal of the stones from the ends of the calices usually causes so much destruction of renal tissue that conservation is inadvisable. The complete removal of multiple small stones situated in different portions of the kidney without much injury to the renal tissue is difficult because of failure of localization. Such difficulty is greatly lessened by the aid of renal fluoroscopy. The suggestion made by W. J. Mayo and by Geraghty that large branched stones in both kidneys should be left alone unless the symptoms are so acute as to warrant emergency operation is, in general, followed. In cases of round or smooth stones in both kidneys, however, operative results are usually much better. If stones

course of six months or may not change in a year or two. They are often not due to actual lithiasis, but to deposits of calcium in the tissues, sandy material, pieces of adhesive plaster near the external wound or bits of suture. In case small fragments remain, drainage is usually well established, and they are often passed spontaneously. In two cases in which the kidney was incompletely delivered, definite shadows of stones of 1 cm. in diameter were noted in the postoperative roentgenograms of partially delivered kidneys. It is in these cases that renal films exposed at operation as suggested by Quinby would be particularly valuable. Although this method is simpler and is more widely available, the delay in developing the films and the technical errors which may arise will retard the operation. Furthermore, localization of the stone is much less accurate.

As previously stated, the indications for operation in cases of multiple renal stones vary largely with the individual circumstances. The following cases are illustrative of many of the problems that present themselves.

#### REPORT OF CASES

*CASE 1.—Multiple stones in one kidney and stone in the lower portion of the ureter on the same side.*

A man, aged 27, complained of having had repeated colic referred to the left loin for several years. Results of physical examination at the clinic were negative. Urinalysis showed 35 pus cells to a field. The renal functional tests were normal. Roentgenograms disclosed the shadow of a branched stone or possibly multiple stones in the area of the left kidney; also two shadows in the region of the lower portion of the left ureter, the larger shadow measuring 1.5 by 1 cm., and the smaller 1 by 1 cm. On cystoscopy, an impassable obstruction was encountered in the left ureter at the ureterovesical juncture. The dye tests indicated moderate reduction in function of the left kidney. The right kidney was normal. The operative procedure consisted of preliminary left ureterolithotomy followed several weeks later by nephrolithotomy with removal of a branched stone and several fragments.

*Comment.*—If stones are present in both ureter and kidney on the same side, it is usually first advisable to remove the stone from the ureter. It has been our experience that a ureteral stone will frequently be displaced immediately following operation on the kidney and may then cause a complicating ureteral obstruction. If the stone is small and situated at the wall of the bladder, manipulation might first be tried although with stones in the kidney as well, only one or two attempts should be made because of possible complicating acute pyelonephritis. With multiple stones of this size ureterolithotomy rather than cystoscopic manipulation is indicated.

*CASE 2.—Stone in the kidney and migratory stone in the ureter on the same side.*

A woman, aged 36, had had intermittent pain referred to the right lower quadrant of the abdomen for three years. Physical examination was negative.

It is now generally recognized that the number of stones discovered at operation often differs from the number of shadows in the roentgenogram; therefore, a method must be employed which will ensure complete removal. Two procedures employed to accomplish this are renal fluoroscopy and roentgenograms made on the operating table. In fact, it is questionable whether a conservative operation for multiple renal stones should be attempted without using one of these methods. We have employed renal fluoroscopy in 370 cases and have found it most useful in the removal of multiple renal stones. Those who are not experienced in the use of renal fluoroscopy claim that it often fails because it does not reveal all the stones. This may occasionally be true of minute fragments from 1 to 2 mm. in diameter. It is rarely true of stones larger than from 2 to 3 mm., if correct technic is employed. Another objection may be raised because of the difficulty experienced in the exact localization of small stones, but this procedure may be greatly aided by the insertion of needles at different angles, under the guidance of the fluoroscope, so that the needle points will approximate at the site of the stone. The objection has been raised that the surgeon is placed in an awkward position when there is a small stone in the end of a calix or in the parenchyma which in spite of skill and patience he is unable to find. As a result, either considerable mutilation of the kidney may be necessary before the stone is found and removed, or it may be advisable to remove the kidney rather than to let the stone remain. There are limits to the extent of renal injury justified in searching for a fragment of stone, and it may occasionally be advisable to leave a small stone fragment rather than injure the kidney further. We have observed several cases in which a small stone was left pocketed at the end of a calix after multiple stones had been removed from the kidney, and on reexamination years later, the stone had not increased in size, had not caused symptoms, and the function of the kidney was almost normal. Leaving the stone, however, is justifiable only in selected cases of this kind. It is true that unless the kidney can be delivered above the level of the abdominal wall, it may be difficult to see it clearly, and yet if the patient is thin, it is remarkable how clearly the kidney can be seen even though not completely delivered. This difficulty has been observed in approximately 15 per cent of all cases.

No method of diagnosis is infallible, but in a review of the 370 cases of renal lithiasis in which renal fluoroscopy was employed, we have found shadows in postoperative roentgenograms in only 21 cases or 6 per cent. In most of these cases, the kidney was incompletely delivered. In several cases, the shadows were doubtful. In fact, minute shadows of no surgical significance are not infrequently observed in the roentgenogram taken soon after operation. Such shadows may or may not be associated with any symptoms and may either disappear in the



figure 1, the shadows of the two stones are visible. one in the right kidney and the other in the right ureter at the level of the third lumbar vertebra.

**CASE 3.**—*Stone in the kidney and pyonephrosis, and stone in the lower portion of the ureter, indicating nephro-ureterectomy.*

A man, aged 22, gave a history of recent attacks of pain referred to the upper part of the left side of the abdomen, with pyuria and hematuria. Physical examination revealed tenderness over the area of the left kidney. The phenol-



Fig. 2 (case 3).—Multiple stones in the left kidney and lower portion of the left ureter.

sulphonphthalein return was 45 per cent in two hours. The urine contained large quantities of blood and pus. On cystoscopic examination, there was evidence of marked reduction in function of the left kidney and an obstruction impassable to the catheter in the lower portion of the left ureter. Roentgenograms disclosed multiple scattered branched stones in the area of the left kidney and multiple large stones in the lower portion of the left ureter. An anterior incision was made, and the lower end of the ureter was freed and ligated. Later nephrectomy was performed through a lateral incision, and the ureter was drawn out with the kidney.

Urinalysis was negative save for a few pus cells. Roentgenograms showed one shadow 1 cm. in diameter in the area of the right kidney and another 1.5 cm. in diameter in the region of the right ureter at the level of the fifth lumbar vertebra. Unsuccessful attempts were made to remove the ureteral stone by manipulation. It was then decided to displace it upward by means of a ureteral catheter introduced through the cystoscope so that both stones could be removed through the same incision at operation. This was done while the patient was under anesthetic just before the incision was made over the area of the right kidney. Pelviolithotomy was then performed, with removal of both stones through the same incision.

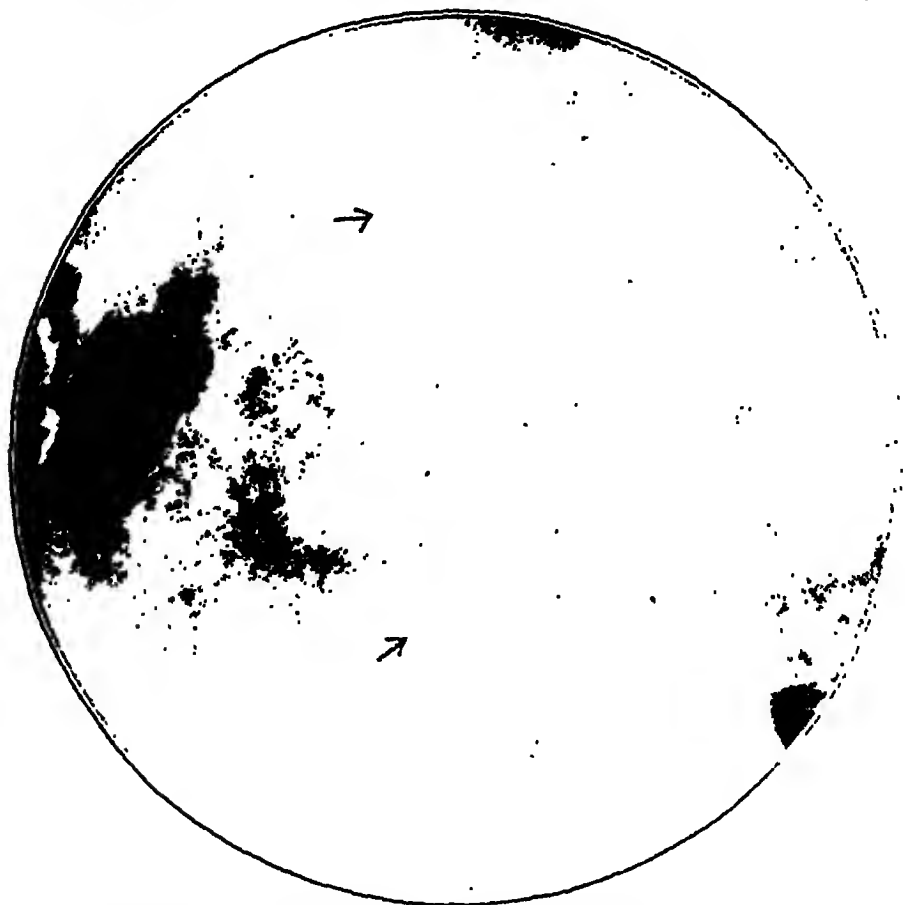


Fig. 1. (case 2).—Two stones, one in the right kidney and the other in the right ureter at the level of the third lumbar vertebra.

*Comment.*—The patient was saved from the ordeal of a possible second operation by this simple maneuver. It is evident that such manipulation would be possible only with a migratory stone and in the presence of a dilated ureter. Removal of a stone situated in the middle third of the ureter by means of the usual methods of ureteral dilatation is usually difficult and possible of accomplishment only after repeated trials and long delay. In the presence of two stones favorably situated the operative procedure here employed is usually to be preferred.

**CASE 5.**—*Massive bilateral nephrolithiasis, symptomless and inoperable.*

A man, aged 20, gave a history of a slight dull ache in the right side of the abdomen for the last six months. There were no urinary symptoms. Results of physical examination were negative, except that urinalysis disclosed 40 pus cells to a field. Roentgenograms showed massive multiple stones in the areas of both kidneys and a single stone in the area of the bladder. The phenolsulphonphthalein output was 35 per cent in two hours, the blood urea was 38 mg. for each 100 cc. Cystoscopic examination showed the function of both kidneys to be slightly reduced and equal. The clinical diagnosis was bilateral nephrolithiasis with



Fig. 3 (case 4).—Stone in the ureter, extra-ureteral stones, and multiple stones in the area of the left kidney.

large branched stones filling the pelvis of the kidneys, stone in the bladder, and moderate renal insufficiency. A stone 4 by 3 cm. was removed from the bladder by litholapaxy.

*Comment.*—The destruction of renal tissue and the possibility of renal fistulas resulting from the removal of multiple renal stones of this type contraindicate surgical procedure unless the symptoms are so severe that life is practically unbearable. Fortunately, it is rare that large coralliform stones are the cause of acute symptoms; occasionally

*Comment.*—In case of multiple stones in the kidney and ureter, and destruction of renal function, combined nephro-ureterectomy is advisable. The patient's condition may occasionally make it advisable to perform nephrectomy first and ureterolithotomy later. Large multiple stones in the ureter, if not removed, may cause considerable local infection. A widely dilated and infected ureter may act as a pocket of infection and should also be removed. If the stone is single and not larger than 1 cm., it can usually be left in situ for the time being. The majority of such stones will not cause further trouble, but should be removed if pocketing of regurgitated urine develops. Shadows of multiple stones in the left kidney and lower portion of the left ureter may be seen in figure 2.

*CASE 4.*—*Multiple stones in one kidney and stone in the lower portion of the ureter on the other side.*

A man, aged 32, had had repeated attacks of pain in the right lumbar area with anterior radiation during the last two years. The results of a general examination were negative. Urinalysis disclosed 50 pus cells to a field. Roentgenograms contained shadows suggestive of stone in the area of the right portion of the ureter, 1.5 by 1 cm. in diameter, probable phleboliths and shadows of multiple stones in the left kidney, the larger 2 by 2 cm. in diameter. On cystoscopic examination, the urine from both ureteral orifices was clear, and the function of both kidneys was equal and almost normal. An unsuccessful attempt was made to remove the stone from the right ureter by manipulation. At operation, right ureterolithotomy was first performed and two weeks later left pelvicolithotomy.

*Comment.*—With stone in the ureter on one side and multiple stones in the kidney on the other side, as in this case, the indications for surgical intervention are the same as in cases of bilateral nephrolithiasis; in other words, the side which presents the most acute recent symptoms should usually be operated on first. In this case, the indication was to remove the stone in the right ureter first. Its removal by means of cystoscopic manipulation might be tried, but because of the danger of subsequent pyelonephritis and because of multiple stones in the kidney on the other side, only one or two attempts should be made. The possibility of one of the stones in the left kidney becoming displaced and obstructing the ureter with resulting anuria must always be considered. If, therefore, the acute symptoms were caused by the renal stone, nephrolithotomy should be performed first, and later manipulation of the stone in the other ureter. In figure 3, the shadow of the ureteral stone is included in the outline of the ureter which, together with the pelvis, is moderately dilated. The other shadows are shown to be extra-ureteral. Shadows of multiple stones are visible in the area of the left kidney.

*Comment.*—In case of multiple small stones in the renal pelvis, there should not be any unnecessary delay in operating because of the danger that one of the stones may pass into the lower portion of the ureter. In such a case, if the stone cannot be removed easily by manipulation, the extra operation is indicated. It is remarkable how often the smaller renal stones will pass into the ureter while the patient is under observation, apparently influenced by the purging and manipulation incident to roentgenography and cystoscopy. Manipulation of a

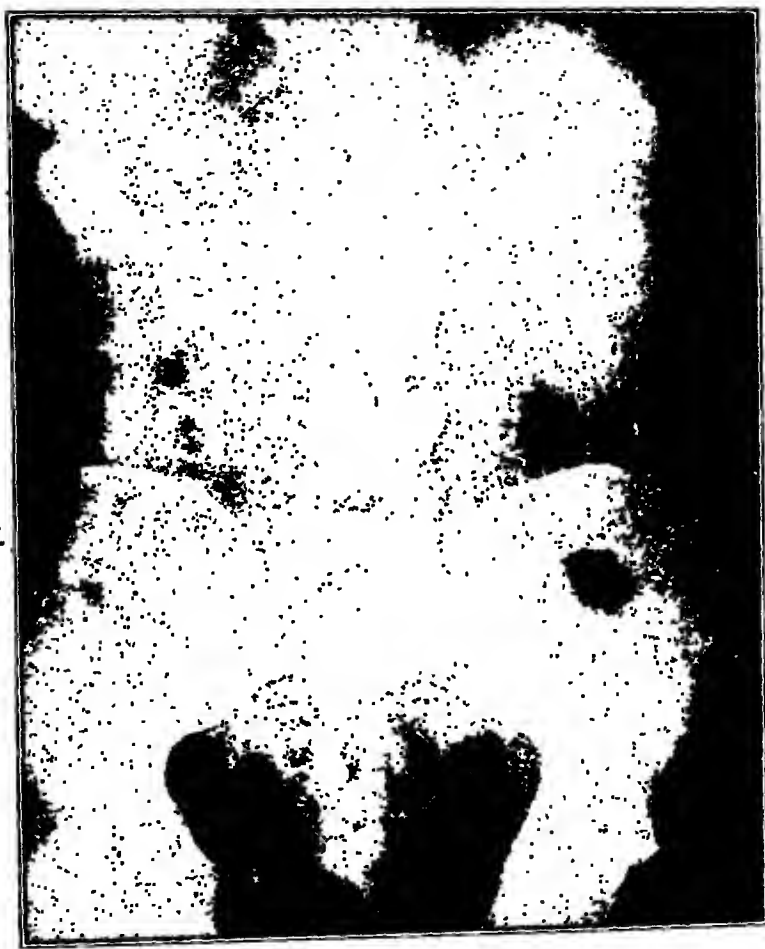


Fig. 5 (case 6).—The stone over the twelfth rib on the right side moved into the lower portion of the ureter.

stone in the lower portion of the ureter in the presence of multiple stones in the kidney is more likely to be followed by acute renal infection than in uncomplicated cases. In figure 5 the smaller stone shadow, which appeared over the twelfth rib on the right side, has now moved into the lower portion of the ureter.

*CASE 7.—Bilateral nephrolithiasis: age as a factor in determining operation.*

A rather feeble man, aged 68, had had dull pain in the left lumbar area at intervals for four years. He had also experienced similar pain in the right flank on several occasions during the last year. Results of physical examination were

a fragment breaks off and obstructs the ureter. Ureterolithotomy or cystoscopic manipulation should then be performed in selected cases. The shadows of multiple branched stones, filling the pelvis and calices of both kidneys, and of the stone in the bladder are shown in figure 4.

*CASE 6.—Bilateral stones, multiple in one kidney with single stone in the other.*

A man, aged 43, gave a history of repeated attacks of colic in the areas of both kidneys, more recently on the right side. Results of physical examination were negative, except for slight tenderness over the right kidney. Urinalysis



Fig. 4 (case 5).—Multiple branched stones filling the pelvis and calices of both kidneys, and stone in the bladder.

showed 32 pus cells to a field. The output of phenolsulphonphthalein was 20 per cent in two hours and the blood urea was 64 mg. for each 100 cc. Roentgenograms showed one large and one small shadow in the area of the right kidney and a single medium-sized shadow in the area of the left kidney. While the patient was being observed and a cystoscopy performed, the smaller stone passed from the right kidney to the lower portion of the ureter. It was necessary to perform a right ureterolithotomy at once. A right pyelolithotomy was performed several weeks later.

cal examination revealed tenderness over both kidneys. The two hour output of phenolsulphonphthalein was 45 per cent. Roentgenograms showed a huge, branched stone and multiple smaller stones in the area of the left kidney and two stones, 1.5 by 1 cm. in diameter, in the area of the right kidney. The outline of the right kidney in the roentgenogram apparently indicates hypertrophy. Cystoscopic examination showed normal function of the right kidney and only slight function in the left. Right pelviolithotomy was performed, followed by left nephrectomy.

*Comment.*—In cases of bilateral stones of this type, in the absence of recent acute symptoms, it is usually advisable to operate first on the



Fig. 7 (case 8).—Huge branched stone and multiple small stones in the area of the left kidney, and two small stones in the area of the right kidney.

kidney that functions better so as to take advantage of the remaining function of the other kidney. After the function of the better kidney has returned to normal, the other kidney can be more safely removed. In this case, immediate right pelviolithotomy was indicated, even though the size of the stone was favorable for spontaneous passage. Under the circumstances, the danger of ureteral obstruction by a migrating ureteral stone is obvious. In figure 7 the shadows of a huge branched stone and multiple small stones appear in the area of the left kidney, and the shadows of two small stones in the area of the right kidney.

negative. Urinalysis showed 60 pus cells to a field. The two hour phenolsulphonphthalein output was 30 per cent, and the blood urea was 58 mg. for each 100 cc. Roentgenograms revealed bilateral nephrolithiasis and multiple round stones in both kidneys. In the left kidney, the largest shadow was 3 by 4 cm., with many small shadows. In the right kidney, the largest shadow was 2 by 3 cm.; there were multiple smaller shadows. Cystoscopic examination demonstrated that the comparative function of the two kidneys was greatly reduced, that of the left kidney being somewhat better than that of the right. It was thought inadvisable to operate on this patient because of lack of acute symptoms and also because of his age.



Fig. 6 (case 7).—Multiple bilateral renal stones.

*Comment.*—If the patient had been 20 or 30 years younger, operation might have been indicated, since his vitality and the life expectancy might then have justified the risk. The shape of the stones might have permitted operation. The comparatively round or smooth stones, even though multiple, would not have necessitated much destruction of tissue. Figure 6 shows shadows of multiple, bilateral renal stones.

*CASE 8.*—*Bilateral nephrolithiasis with one kidney practically normal and the other normal*

A man, aged 25, had had attacks of severe pain in both kidneys for the last 7 years. Recently the pain had been referred entirely to the right side.



kidney with the better function first, and, if indicated, to remove the other kidney later. Since the pain in this case was practically the same on both sides, it was deemed advisable to operate on the right kidney first because of its better function, and to remove the stone in the ureter before pelviolithotomy was attempted. As the stones were not branched and, therefore, were not wedged into the calices, they could be removed without much injury to the renal tissue. The indefinite hazy shadow adjacent to the shadows of the larger stones is explained by sandy material. Even though this is not completely removed, there is seldom danger that it will act as a nucleus for the formation of other stones if adequate drainage is established. In figure 8 may be seen the shadows of multiple stones in the areas of both kidneys. The stone in the lower portion of the left ureter is not visible in the roentgenogram.

*CASE 10.—Bilateral nephrolithiasis: multiple small stones in one kidney and a single small stone in the other.*

A woman, aged 32, gave a history of intermittent colic referred to the right loin, accompanied by pyuria, and chills and fever during a period of two and a half years. Several small stones had passed during these attacks. There were no symptoms referable to the left kidney. The results of a general physical examination were negative. The roentgenograms contained multiple scattered shadows of stones varying in size from 0.5 to 1 cm. in the area of the right kidney, and the shadow of a single stone 1 cm. in diameter in the area of the left kidney. On cystoscopic examination, the function of both kidneys was found to be normal and equal, and by means of urography the shadows were shown to be intrarenal. A diagnosis was made of bilateral nephrolithiasis, multiple small stones in the right kidney and a single stone in the left kidney. Combined nephropelviolithotomy was performed, and five cortical stones were removed from the right kidney. Fluoroscopic examination on the operating table showed that the kidney was free from stones. This observation was corroborated by a postoperative roentgenogram. The stone from the left kidney passed after an attack of colic. Cystoscopic examination one month later showed the function of both kidneys to be normal.

*Comment.*—It was thought advisable in this case to remove the stones from the right kidney only because the stone in the left was single, was not causing acute symptoms and was small enough to pass. The removal of multiple small stones scattered widely in the kidney may be exceedingly difficult, but with the aid of renal fluoroscopy their complete removal with a minimum of renal injury is usually possible. In figure 9 are seen the shadows of multiple small stones in the right kidney and a small single stone in the left kidney.

*CASE 11.—Multiple, bilateral stones with conservative operation indicated for both kidneys.*

A man, aged 48, gave a history of having passed stones and sand at intervals since he was 8 months old. Pain was always confined to the left side of the abdomen and had been more acute recently. The urine had been cloudy for years. The results of the physical examination were negative except that acute tender-

**CASE 9.—Operable bilateral nephrolithiasis, together with stone in the ureter.**

A woman, aged 47, came to the clinic with a history of repeated attacks of colic referable to the left renal area and occasional dull pain in the right. The results of a general physical examination were negative. The roentgenograms showed shadows of multiple stones in the area of the right kidney, and one or more in the area of the left kidney, as well as a shadow 2 mm. in diameter in the area of the lower portion of the left ureter. Cystoscopic examination showed the function of both kidneys to be somewhat less than normal, the function of the right being slightly better than that of the left. A stone was seen partially protruding from the left ureteral orifice: this was cut, and it subsequently passed.



Fig. 8 (case 9).—Multiple stones in the areas of both kidneys.

Right pelvolithotomy was performed and a single staghorn stone was removed from the kidney, together with much sandy material. Subsequently, a left pelvolithotomy was done, and a stone, 2 by 2 cm. in diameter, a number of small stones and some sandy material were removed. Two months after operation the function of both kidneys was normal and equal. Subsequent roentgenograms were negative.

*Comment.*—In the presence of bilateral nephrolithiasis, it is usually advisable to operate first on the kidney causing recent acute symptoms. If the symptoms are not acute, it is usually advisable to operate on the

stone remain in the left kidney, but they are in the ends of the calices, where they will probably cause little further injury. Should they increase in size, they can be more easily found and removed later. The fact that twelve stones were removed from the right kidney and that a postoperative roentgenogram was negative attest to the value of fluoroscopy. Postoperative cystoscopy showed marked improvement in the function of both kidneys. The possibility for improvement in renal function following operation for multiple stones is greater when localized areas of infection are present than when they are not.



Fig. 10 (case 12).—Two large stones in both lower ureteral areas, with lead catheters adjacent to them.

*CASE 12.—Bilateral large ureteral stones.*

A man, aged 28, had had dull pain, referred to the areas of both kidneys, pyuria and intermittent spells of fever for many years. Physical examination revealed cachexia and severe anemia. Urinalysis showed a large amount of pus. The phenolsulphonphthalein return in two hours was 15 per cent, and the blood urea 44 mg. for each 100 cc. Roentgenograms showed two large shadows in the area of the bladder, which might have been caused by stones in the diverticula of the bladder or in the ureters. On cystoscopic examination, multiple diverticula

ness was evident over the left lumbar area. Urinalysis revealed pus in large quantities. The two hour output of phenolsulphonphthalein was 15 per cent; and the blood urea was 52 mg. for each 100 cc. Roentgenograms showed multiple shadows scattered over the areas of both kidneys. On cystoscopic examination, the urine from both kidneys was found to be cloudy, and the function of both kidneys to be greatly and equally reduced. A diagnosis was made of multiple stones in both kidneys with reduced function and infection. Eight stones were removed from the left kidney by combined nephropelviolithotomy. The kidney was three times the normal size and contained a great deal of pus. Although



Fig. 9 (case 10).—Multiple stones in the right kidney and a single stone in the left kidney.

fluoroscopic examination showed two remaining shadows, it was considered advisable not to carry on the search since the patient was weak and the removal of the stones would have necessitated much destruction of renal tissue. Subsequently a right nephropelviolithotomy was performed and twelve stones were removed. Postoperative roentgenograms showed two fragments of stone remaining in the left renal area and none in the right.

*Comment.*—The case illustrates the extent to which conservative operation can be successfully carried out in bilateral multiple nephrolithiasis by employing renal fluoroscopy. It is true that two fragments of

the upper portion of the ureter and pelvis. An attempt should be made to find the smaller stones first, since the larger stones can be picked up readily. Fortunately, in this case the stones passed following cystoscopic manipulation, although their presence caused a ureteral fistula for a period of several weeks.

*CASE 14.—Stone in kidney, ureter and bladder.*

A man, aged 38, was examined at the Clinic in February, 1925. Five years previously, he had had an attack of sharp colic referred to the upper right quadrant of the abdomen and to the lumbar area, which required several hypodermic injections for relief. Since then he had had similar attacks of pain at intervals of from two to six months. Three years previously, a stone, about 0.5 by 1 cm., had passed with hematuria. One week before he came to the clinic, the pain had been referred to the left kidney, with anuria for two days. A roentgenogram made elsewhere showed the shadows of stones in both kidneys. Recently he had complained of anuria and nausea, but he was otherwise normal. Urinalysis showed the presence of a moderate number of pus cells and red blood cells. The roentgenograms contained what appeared to be shadows of stones in the bladder, right ureter and right kidney. There was no trace of phenolsulphonphthalein in two hours; the blood urea was 282 mg. for each 100 cc., and blood creatinine was 7. A low protein diet, hot packs and forced fluids were prescribed. In three days, the blood urea dropped to 112 and the creatinine to 4.8. The diet was continued, and a week later the blood urea was 36 and the phenolsulphonphthalein return 30 per cent. On cystoscopic examination, a diagnosis was made of stone in the bladder, 2 by 1.5 cm., which had apparently recently passed from the left kidney; this explained the rapid drop in the blood urea. A urogram localized a shadow in the middle third of the right ureter, and the shadow in the kidney was included in the outline of the renal pelvis. The function of the right kidney was moderately reduced. The stone was removed from the bladder by litholapaxy. Through a right posterolateral incision, the ureteral stone situated at the middle portion of the ureter was worked back into the pelvis and removed, together with the stones in the kidney.

*Comment.*—The fact of greatest interest in this case was the evidence of marked renal insufficiency. In cases of multiple renal stones, the question not infrequently arises, whether operation is indicated in the presence of high blood urea retention. If there is acute ureteral obstruction, immediate operation would, of course, be advisable. In the absence of such obstruction, unless evidence of renal insufficiency can be materially eliminated by placing the patient in the hospital and prescribing a low protein diet, forced fluids and elimination, the advisability of operation is questionable. The anuria and evidence of retained nitrogenous elements in this case can be explained by the recent blockage of the left kidney by the ureteral stone, now in the bladder, and the presence of multiple stones in the right kidney and ureter. It is interesting to note the limits that the urea can attain as a result of urinary retention and then return to normal following reestablishment of urinary drainage and other treatment. In the presence of coincident stone in the bladder and kidney, litholapaxy is usually indicated, and it saves the

were found, but stones were not visible. A cystogram showed the outline of the stones extending beyond the outline of the bladder, so that it was evident that they were intra-ureteral. This was further corroborated by lead catheters introduced into the ureters, which were found in a urogram to be adjacent to and partially coiled around the stone. A diagnosis of two large bilateral ureteral stones and multiple diverticula of the bladder was made. At the operation, bilateral ureterolithotomy was performed, the right side being operated on first. Later the diverticula were resected.

*Comment.*—It is evident that any attempt at manipulation of stones of this size in a ureter is contraindicated. When complicated by diverticula in the bladder, as in this case, they should be removed before the latter are resected, because of the possibility of ureteral obstruction. Furthermore, renal function should be as nearly normal as possible before major operation on the bladder is attempted. In figure 10 the outline of two large stones is visible in both lower ureteral areas, with lead ureteral catheters adjacent to them.

*CASE 13.—Multiple stones in ureter; difficulties in removal.*

A man, aged 53, presented himself for examination in April, 1924. In 1915, a stone had been removed elsewhere from the right ureter. In 1916, three small calculi passed while the patient had colic referred to the area of the left kidney. Six months previous to the time he was examined, he experienced severe colic in the left side, and at that time roentgenograms showed a shadow opposite the third lumbar vertebra and a smaller one in the kidney. Since then a dull, dragging feeling had been noted in the left flank in the morning. Roentgenograms showed a shadow under the fourth transverse process on the left side, apparently due to multiple calculi. Urinalysis showed the presence of a few microscopic pus cells, and tests of renal function were negative. On cystoscopic examination, an impassable obstruction was met by the catheter 15 cm. above the ureteral orifice. A ureterogram showed slight dilatation of the left lower third of the ureter. There was no evidence of iodide above the shadow of the larger stone. A diagnosis was made of multiple stones in the lower third of the ureter, the largest being 2 by 2 cm., with two smaller stones just above it.

Ureterolithotomy was performed, and only one stone corresponding in size to the larger shadow could be found. The ureter was dilated above this, and it was thought possible that the smaller stones might have passed up into the kidney. A persisting fistula remained in the ureter for several weeks following the operation. Postoperative roentgenograms showed two small stones in the lower third portion of the left ureter. Several ureteral catheters were introduced into the ureter full length and fastened in it. Following repeated manipulations, both stones passed.

*Comment.*—With multiple stones in the ureter, and particularly if the lower one is the larger and impacted, it is logical to assume that the ureter above is greatly dilated. In such cases extra precautions should be taken not to permit the smaller stones to escape from the field of operation. With the relaxation caused by anesthesia and with the patient in the Trendelenburg position, even though the proximal portion of the ureter is partially clamped, a small stone may escape into

never had any urinary symptoms. The results of a general examination were negative, including tests of renal function. Urinalysis disclosed an occasional pus cell. A renal roentgenogram contained two shadows apparently in the area of the left kidney, the larger being 1 by 1 cm. On cystoscopic examination and pyelography, an anomalous pelvis of a fused left kidney was found. The original shadows of the stones were included in the outline of the pelvis. Anomalous lateral insertion of the ureter with evidence of abnormal rotation of the pelvis was typical of a fused kidney. A subsequent pyelogram of the right side showed a similar condition. The function of both kidneys was practically normal. A diagnosis was made of multiple stones in the left pelvis of a fused kidney.

The fused kidney was revealed through an anterior incision. The pelvis of the left half of the kidney was extremely dilated, and a stone, 1.5 by 1.75 cm., was removed. The stone was shaped like a dumb-bell, giving the appearance of a second stone in the preoperative roentgenogram. Other stones could not be found on exploration.

*Comment.*—Multiple stones in a fused kidney offer peculiar complications in judging the necessity of surgical intervention. If the stones are large and branched, filling the pelvis of the kidney, without causing significant symptoms, an operation is hardly indicated. It must be admitted that the difficulties of operation in a fused kidney are greater than in the normal kidney. As a rule, the anterior approach with conservative operation in a fused kidney is preferable to the posterior incision. The difficulty in delivering the kidney and in completely removing the stone is necessarily greater. Unless the patient is unusually thin, it is impossible to employ renal fluoroscopy in the presence of a fused kidney, and the use of roentgen-ray films on the operating table might be applicable.

Stones shaped like dumb-bells frequently give the appearance of multiple stones. One must be certain, however, that another stone is not present, even though the shape of the stone is such that it could cast two shadows. The position of a stone of this type in itself would be suggestive of renal anomaly, since multiple stones of this kind usually are not present in the ureter. In a fused kidney, they are generally near the median line, as in this case. The appearance of the pyelogram, and particularly the insertion of the ureter and the rotation of the calices, are typical of horseshoe kidney, and it should be easily recognized.

In figure 11 the pelvis of the left kidney is visible, with two original shadows obscured by the pelvis, which is slightly dilated. Failure of complete rotation of the pelvis is typical of fused kidney. The calices are dilated.

patient from undergoing an operation. Under such circumstances, the stone in the bladder is usually of renal origin. Also of interest in this case was the ability to work the stone in the ureter up into the pelvis so that it could be removed together with the renal stone through one incision. This, of course, is possible only when the stone is not too large and irregular and when the ureter is large enough to permit it. As seen in the urogram, the ureter was hardly large enough to permit this, but it was probably not completely distended. The pelvis and



Fig. 11 (case 15).—Two original shadows obscured by the pelvis of the left kidney.

calices may be normal in spite of the presence of a stone in the kidney and ureter.

*CASE 15.—Stones in the left half of a fused kidney.*

A man, aged 39, presented himself for examination at the clinic in July, 1924. His gallbladder and appendix had been removed at another hospital in 1921. Eight months prior to examination, he first noticed sharp pain originating in the lower left abdominal quadrant and radiating through to the back and downward into the area of the bladder. Four severe attacks during the last three months before he came to the clinic had required the administration of morphine. He had



never had any urinary symptoms. The results of a general examination were negative, including tests of renal function. Urinalysis disclosed an occasional pus cell. A renal roentgenogram contained two shadows apparently in the area of the left kidney, the larger being 1 by 1 cm. On cystoscopic examination and pyelography, an anomalous pelvis of a fused left kidney was found. The original shadows of the stones were included in the outline of the pelvis. Anomalous lateral insertion of the ureter with evidence of abnormal rotation of the pelvis was typical of a fused kidney. A subsequent pyelogram of the right side showed a similar condition. The function of both kidneys was practically normal. A diagnosis was made of multiple stones in the left pelvis of a fused kidney.

The fused kidney was revealed through an anterior incision. The pelvis of the left half of the kidney was extremely dilated, and a stone, 1.5 by 1.75 cm., was removed. The stone was shaped like a dumb-bell, giving the appearance of a second stone in the preoperative roentgenogram. Other stones could not be found on exploration.

*Comment.*—Multiple stones in a fused kidney offer peculiar complications in judging the necessity of surgical intervention. If the stones are large and branched, filling the pelvis of the kidney, without causing significant symptoms, an operation is hardly indicated. It must be admitted that the difficulties of operation in a fused kidney are greater than in the normal kidney. As a rule, the anterior approach with conservative operation in a fused kidney is preferable to the posterior incision. The difficulty in delivering the kidney and in completely removing the stone is necessarily greater. Unless the patient is unusually thin, it is impossible to employ renal fluoroscopy in the presence of a fused kidney, and the use of roentgen-ray films on the operating table might be applicable.

Stones shaped like dumb-bells frequently give the appearance of multiple stones. One must be certain, however, that another stone is not present, even though the shape of the stone is such that it could cast two shadows. The position of a stone of this type in itself would be suggestive of renal anomaly, since multiple stones of this kind usually are not present in the ureter. In a fused kidney, they are generally near the median line, as in this case. The appearance of the pyelogram, and particularly the insertion of the ureter and the rotation of the calices, are typical of horseshoe kidney, and it should be easily recognized.

In figure 11 the pelvis of the left kidney is visible, with two original shadows obscured by the pelvis, which is slightly dilated. Failure of complete rotation of the pelvis is typical of fused kidney. The calices are dilated.



others have emphasized the importance of the pylorus in relation to chronic ulcer in man. In Fenwick's<sup>7</sup> statistics from human beings 75 per cent of the chronic gastric ulcers occur in this region, while, experimentally, acute lesions frequently show a delay in healing in the pylorus. More trauma is produced in this area from food and gastric juice than in other areas of the stomach (Friedman and Hamburger,<sup>8</sup> Morton<sup>9</sup> and others).

Konjetzny<sup>10</sup> discussed the importance of injury to the mucosa from food and reported some interesting observations on weaned calves. Gastritis, multiple erosions and chronic ulcers were found in the stomach after the diet was changed from milk to rough food. These lesions healed when the calves were again put on a milk diet. He concluded that trauma was most important and that the gastric juice was of minor importance in the etiology of these lesions. Baggio<sup>11</sup> also produced chronic gastric ulcer experimentally when he fed a coarse diet mixed with 3 per cent hydrochloric acid, but he failed to produce ulcers when he fed acid alone. His experiments, however, are too few to permit of any definite conclusions.

Many types of operations have been performed for the purpose of studying the influence of acid on ulcers, by increasing the secretion of acid or prevention of neutralization by deflection of the duodenal contents into the ileum. Other methods have been the injection of quantities of acid into the stomach. Matthes,<sup>12</sup> in 1893, used this method in one dog and produced a delay in the healing of an acute ulcer. In investigations on monkeys and cats, Bolton<sup>13</sup> made a more extensive study of this method of artificial hyperacidity. He fed the animals acid solutions varying from 0.18 to 1.5 per cent. He concluded that the destructive power of gastric juice was due to the hydrochloric acid present and that the acid was usually a factor in the initiation of an ulcer.

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# EFFECTS OF INJECTIONS OF ACID AND TRAUMA ON JEJUNAL TRANSPLANTS TO THE STOMACH

WILLIAM J. GALLAGHER, M.D.

Seymour Coman Fellow in the Department of Physiology of the University of  
Chicago and the Department of Surgery of Rush Medical College  
of the University of Chicago

CHICAGO

Experimental data are presented on further studies on intestinal segments transplanted to the stomach. Particular study has been made of the influences of the chemical and traumatic factors in the etiology of ulcer.

The almost constant observation of hydrochloric acid in clinical peptic ulcer has frequently led to the conclusion that it is an essential element in its production. Experimentally, however, it has been rather definitely established by many workers that uninjured intestinal mucosa is unaffected by exposure to the digestive action of gastric juice.

Isolated segments of intestine, with their blood supply intact, transplanted to the stomachs of dogs, remained unchanged in the experiments of Hotz<sup>1</sup> and Licini.<sup>2</sup> Later, Dragstedt and Vaughn<sup>3</sup> showed that various parts of the intestinal tract, kidney and spleen transplanted to the stomach remained normal when subjected to the digestive action of gastric juice for long periods. In an experimental study of transplants to different areas of the stomach, De Takats and Mann<sup>4</sup> obtained a small percentage of chronic ulcers in patches on the lesser curvature of the stomach near the pylorus. The percentage of chronic ulcers was even greater, when a surgical duodenal drainage was also performed (Morton<sup>5</sup>). The acid-alkali imbalance produced in the stomach by the latter operation and the mechanical stress to the patch on the lesser curvature were the causative factors in these ulcers. Aschoff<sup>6</sup> and

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## EXPERIMENTAL METHODS

Normal, healthy dogs were used. All operations were done aseptically under ether and morphine anesthesia. After recovery from the operation, the animals were given a diet of meat, bones, bread and water. The nutritional condition remained good in most of the animals until ulcers developed. The acid solutions had a tendency to decrease the animal's appetite, particularly those of a higher concentration. Variations in the amount and frequency of the injection of acid usually obviated this condition.

Openings about 8 by 4 cm. were made in different areas of the anterior or posterior walls of the stomach. Many of these openings were made close to the lesser and greater curvatures and about 4 cm. from the pyloric sphincter. A suitable length about 8 to 13 cm. of a freely movable part of the jejunum, with its blood supply maintained, was sutured into the selected areas of the stomach. The ends of the isolated segment were closed by catgut pursestring sutures. The continuity of the bowel was reestablished by end to end anastomosis, and in several by lateral anastomosis. The segment formed a part of the stomach wall with pouching of the pursestringed ends into which gastric juice and food would gravitate.

In three animals, after healing was complete, 0.62 per cent acid barium solution was injected; roentgenograms were then taken to determine the condition and position of the transplant and its effect on the emptying time of the stomach.

Exploratory operations were performed at various times from 12 to 112 days after transplantation. In five of the animals acute traumatic lesions of the transplant mucosa were made in various locations. Young's clamps were applied in one or two areas for from thirty-five to fifty minutes to produce these lesions. (In previous experiments<sup>14</sup> these pressures were found to produce acute penetrating ulcers of the duodenum jejunum.) In a group of seven animals, five of which had traumatic lesions, injections of hydrochloric acid were started two days after the production of the lesion of the transplant mucosa. The injections of acid were given through an Ewald stomach tube without an anesthetic for from twenty-four to fifty-eight days. In some instances the acid solution was given twice daily in amounts of from 200 to 225 cc. The concentrations of the solution were 0.22, 0.29 and 0.62 per cent. The percentages were obtained by using 3, 3.5 and 9 cc., respectively, of a 35 per cent hydrochloric acid added to sufficient water to make 550 cc. (these solutions were titrated with decinormal sodium hydroxide and found to agree with the foregoing percentages). If the solutions were injected too rapidly or in quantities of more than 225 cc., vomiting would occur immediately. This was especially true with the higher percentage of acid solution. Aspirations of the stomach from four to five hours after injection frequently gave negative results except in those animals in which a retention had been present.

*Results.*—Twenty-four animals with jejunal transplants were studied for a period of from 12 to 154 days. Several animals that developed an intussusception of the lateral anastomosis were not included in the group. Chronic intussusception was found in four of the group, resulting in some emaciation, but the transplant remained normal.

Seventeen animals were used for control study. Chronic ulcers occurred on the proximal and distal ends of the transplant in two, fifty-four and sixty-nine

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TABLE 1.—*A Series of Jejunal Loop Transplants to Stomach*

Ex- per- iment	Date of Opera- tion	Location of Transplant	Exploratory Operation	Interval, Days	Remarks
1	2/25/27	Posterior wall near greater curvature	Intestinal obstruc- tion at site of anastomosis	151	Normal transplant mucosa; dilatation of duodenum
2	3/ 9/27	Middle of ante- rior wall	Intussusception of intestinal anas- tomosis	48	Transplant normal
3	4/10/27	Posterior wall near lesser curvature	Intussusception of lateral anas- tomosis	82	Emaciation, normal trans- plant mucosa
4	4/10/27	Middle of pos- terior wall	Transplant healed	12	Distemper developed
5	4/ 8/27	Posterior wall near greater curvature	Two chronic ulcers on ends of trans- plant 1.2 by 1 and 0.3 by 0.3 cm.	60	Much scar tissue at base of distal ulcer
6	4/ 9/27	Posterior wall near lesser curvature	Normal transplant mucosa	53	Marked narrowing of end to end anastomosis; some emac- iation
7	4/30/27	Anterior wall, lesser curva- ture near pylorus	Normal transplant mucosa	72	Some emaciation
8	4/22/27	Anterior wall, midportion	Chronic ulcer on distal end of transplant 1 by 1 cm.	51	Some emaciation present
9	4/23/27	Middle of an- terior wall	Normal transplant mucosa	44	Developed distemper
10	4/23/27	Anterior wall near greater curvature	Sharp spike of bone perforating distal end of transplant	23	Serosanguinous exudate in per- itoneal cavity; normal trans- plant mucosa
11	5/ 5/27	Anterior wall near lesser curvature	Normal transplant mucosa	45	Obstruction of duodenum due to hair ball
12	7/12/27	Middle of pos- terior wall	Normal mucosa	26	Some emaciation
13	7/ 2/27	Anterior wall near lesser curvature	Normal mucosa	26	Developed distemper
14	6/14/27	Middle of an- terior wall	Normal mucosa	21	Developed distemper
15	7/16/27	Anterior wall near lesser curvature	Normal mucosa	22	Death from anesthesia during exploratory operation
16	7/18/27	Anterior wall near lesser curvature	Spike of bone per- forating distal loop transplant; perforation closed by purse-string suture	42	Animal died one month after exploratory operation; nor- mal mucosa
17	8/ 1/27	Anterior wall near greater curvature	Normal mucosa	14	Condition poor after operation; loss of appetite; died

and 0.6 by 0.3 cm., were found in one animal of the seven, on the proximal and distal ends of the transplant, on the fifty-sixth day of the injections of acid and the one hundred and sixteenth day after operation. The mucosa of the transplant of this animal between the ends was hyperemic, slightly swollen and covered with mucus. This transplant was located on the posterior wall about 2 cm. from the greater curvature, near the pylorus. Edema, some hyperemia and a few petechiae



Fig. 2.—Jejunal loop with chronic ulcers on ends found sixty-nine days after transplantation to posterior wall of the stomach; lateral anastomosis of intestine, containing a fragment of bone in the free end.

were present in the mucosa of four of the animals in the group in which injections of acid were given. An appreciable amount of tenacious mucus was a constant observation in the stomachs and transplants of animals that received acid solutions. Larger amounts were found after the injection of the 0.62 per cent solution than after the use of 0.22 or 0.29 per cent acid. All the acute lesions

days after operation. These transplants were on the posterior and anterior wall of the stomach near the greater curvature. The mucosa was otherwise normal in these as well as the remaining seventeen control experiments. Microscopically, a moderate amount of scar tissue was present in the healed ends of the transplant. There was a marked tendency to pouch formation of the transplant. In a few of the animals, there was a dilatation of the stomach and transplant with a



Fig. 1.—Photograph taken after fixation of stomach in formaldehyde. Stomach and jejunal loop greatly dilated; loop in stomach 151 days; injections of 0.22 acid solution were made daily for 33 days; ulcers were not observed.

tendency to retention. A sharp spicule of bone was found in the distal end of the transplant in two animals. One of the spicules had perforated the transplant with a resulting serosanguinous exudate in the peritoneal cavity. A chronic ulcer, mentioned previously, was found on the end of the transplant of the other animal. In the group in which injections of acid were made, two chronic ulcers, 0.5 by 0.2



TABLE 2.—A Series of Injections of Hydrochloric Acid Into Stomachs with Jejunal Transplants (Acute Traumatic Lesions Produced by Clamp Pressure)

TABLE 2.—A Series of Injections of Hydrochloric Acid Producing Traumatic Lesions										
Experiment	Date of Operation	Location of Transplant	Injection of Hydrochloric Acid			Acute Traumatic Lesion		Interval, Days	Necropsy Results	Remarks
			Per-centage injected,	No. of Days	Date of Operation	Location of Transplant				
18	2/12/27	Posterior wall, middle	0.52	200	33	5/11/27	Distal third	151	Dilated stomach, much mucus present; hyperemic traumatic lesion healed	Edema of lungs from aspiration of acid solution
19	4/13/27	Posterior wall, near greater curvature	0.29	200	53	8/ 5/27	Middle of transplant	154	Edema of transplant mucosa; two chronic ulcers on ends of transplant, 0.5 by 0.2 and 0.8 by 0.3 cm.; mucus in stomach	Frequent vomiting of mucus and acid solution
20	4/15/27	Middle of posterior wall	0.29 0.62	200 twice daily	20 32	.....	.....	50	Edema and petechiae of transplant mucosa; mucus in stomach and traumatic lesion healed	Developed symptoms of acidosis
21	6/11/27	Middle of anterior wall	0.22	200	60	8/10/27	Two areas, middle and lower third	78	Mucus in stomach normal plant; mucosa normal	Frequent vomiting of acid solution
22	7/10/27	Posterior wall near lesser curvature	0.62	200	27	8/ 8/27	Middle	73	Traumatic lesion healed; much mucus present; some edema of transplant mucosa	Slight cellular exudate in mucosa of transplant
23	7/27/27	Anterior wall near greater curvature	0.62	200 twice daily	32	8/10/27	Two areas, middle and proximal portions	41	Healed traumatic lesion; some edema of transplant mucosa; much mucus present	Developed symptoms of acidosis
24	8/ 2/27	Anterior wall near lesser curvature	0.12 0.62	200 twice daily	..	.....	.....	.....	Edema and petechiae of mucosa present; traumatic lesion healed; much mucus in stomach and transplant	Slight cellular exudate in mucosa of transplant; developed symptoms of acidosis

produced by clamps had completely healed leaving little evidence grossly of scar formation. After injection of acid for from three to four weeks, some of the animals developed symptoms of acidosis.

Microscopically, there was a moderate amount of cellular exudate in the mucosa of the transplant of the group which received injections of acid. Goblet cells were found in the mucosa of a few of the transplants.

#### COMMENT

Scar tissue was constantly present in the ends of the transplants, in which chronic ulcers were found in three animals. Consequently, the most important etiologic factor was undoubtedly the nutritional dis-



Fig. 3.—Photomicrograph of chronic ulcer on distal end of transplant shown in figure 2; superficial necrosis with abundant scar tissue in base of ulcer:  $\times 32$ .

turbance present in these regions of the transplant. The location of the segment in the stomach seemed to have little influence on the occurrence of ulcer in these experiments. In those transplants with chronic lesions, the distal lesion was always larger than the proximal one. This is logical, since the distal part was more frequently subjected to trauma from food and perhaps the action of gastric juice.

Several times at exploratory operation and postmortem examination, the distal end of the transplant contained food, bones and gastric juice, while the proximal end was usually empty. The tendency to retention in this portion of the transplant was also observed in the roentgen-ray

those in the control experiments, 112 days after operation and 58 days after the injection of 0.62 per cent hydrochloric acid. In four animals of this group, edema and some hyperemia of the mucosa were noted.

Gastric mucus was a constant observation in the stomachs and transplants of the series in which injections of acid were made. Acute traumatic ulcers of the transplants in six of the series with artificial hyperacidity healed with only slight gross changes. Nutritional disturbance of the ends of the transplants was suggested as the probable important factor to explain the presence of chronic ulcers found in these experiments. The gastric mucus and alkaline secretion of the intestine were considered an important protective influence to the mucosa against the irritant action of the hydrochloric acid solution injected.

#### CONCLUSION

In these experiments the attempt at artificial hyperacidity failed to increase the occurrence of chronic ulcer in the stomach itself, in the scar tissue of the transplant or in the transplant mucosa.

examination, when barium material was observed after the upper part of the transplant was empty. The tendency of the transplant to pouch formation protected the mucosa from the greater trauma from food and the action of gastric juice. It was also a factor in aiding the healing of acute traumatic lesions. Observations were not made on the time of healing of these lesions. Grossly and microscopically the healed lesions were not unlike those found in the duodenum and jejunum in previous experiments. Bolton<sup>15</sup> reported a delayed healing of acute ulcers in the stomach following the injection of solutions of hydrochloric acid.

The constant presence of gastric mucus in the experiments with artificial hyperacidity was, no doubt, with the alkaline secretion of the intestine, a protective influence against the irritant action of the hydrochloric acid. Frequently vomiting of acid solutions, especially those of higher concentration, also decreased the efficiency of this method of hyperacidity. The rapid emptying of the stomach of acid solution (Carlson,<sup>15</sup> Steinberg,<sup>16</sup> Olch<sup>17</sup> and others) still further limited the time of action of the acid on the transplant mucosa. The few changes observed (hyperemia and edema) are in part explained by these factors. The fact that the higher concentration of acid (0.62 per cent) did not produce any greater changes in the transplant mucosa than the lesser concentration solution (0.29 per cent) is further evidence of the protective influence of the various factors mentioned.

In these experiments, trauma, due to operation, and lessened blood supply to the ends of the transplant caused nutritional disturbances which determined the site of the mucosal ulceration.

#### SUMMARY

Chronic ulcers were observed on the ends of two transplants of seventeen animals, in which the blood supply to the loop was maintained. These transplants were on the posterior and anterior wall of the stomach near the greater curvature. The longest period of observation was 154 days.

An artificial hyperacidity was produced by injections of varying concentrations of hydrochloric acid from once to twice daily into the stomach in seven animals, for periods of from twenty-four to fifty-eight days. In one of these, two chronic ulcers were observed similar to

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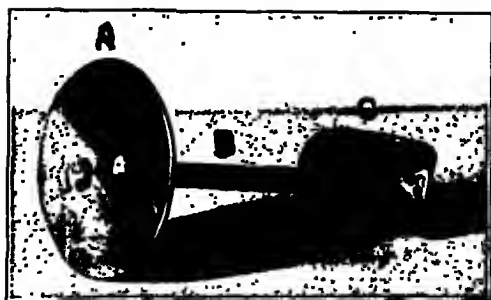


Fig. 2.—Depression in the plate (*A*) for the entrance of the needle into the tubes.



Fig 3.—Dog two weeks after operation. The arrow points to the instrument.

# PHYSIOLOGY OF THE LIVER AND INTESTINE

## METHOD OF STUDY \*

CYRUS F. HORINE, M.D.

BALTIMORE

I shall make a preliminary report on a method for the study of the function of the intestine and liver, with particular reference to the study of the portal blood. This method is for experimental use in animals.

An instrument or permanent cannula is used between the portal vein and the skin of the abdominal wall. It is a gold plated cannula having two tubes.

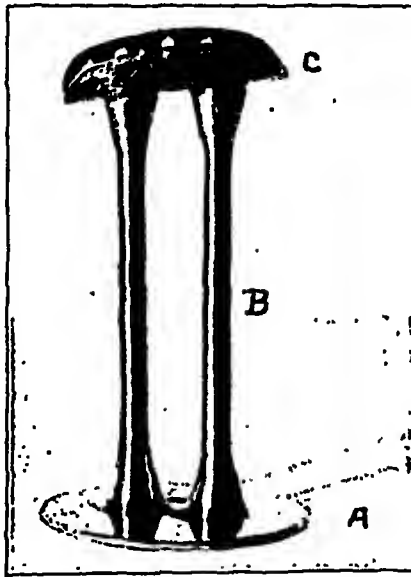


Fig. 1.—Instrument used in experiment.

These tubes barely allow the passage of an 18 gage record needle. Sterling silver tubing is used because it is impossible to plate the lumen of the tube.

The instrument consists of two tubes (*B*) connecting a concave portion (*C*) which is sutured over the portal vein to a round flat plate (*A*). The round flat plate is placed beneath the skin of the abdominal wall. It is about the size of a half silver dollar (fig. 1).

The operation is performed with the animal under general anesthesia. A half moon incision is made in the upper right quadrant. The convex surface of the incision points toward the midline. A longitudinal incision is made through the rectus muscle and peritoneum. The portal vein is exposed, and

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\* From the Department of Surgery, University of Maryland.

A great many dogs were killed because of infections in the wound. This was overcome by placing a silver wire drain (made of twisted strands of silver wire) in the wound, for a period of from two to three days. Otherwise the dogs would develop a collection of serum beneath the skin with a secondary infection of the wounds. The wounds usually heal in from ten days to two weeks, and the vein may then be aspirated.

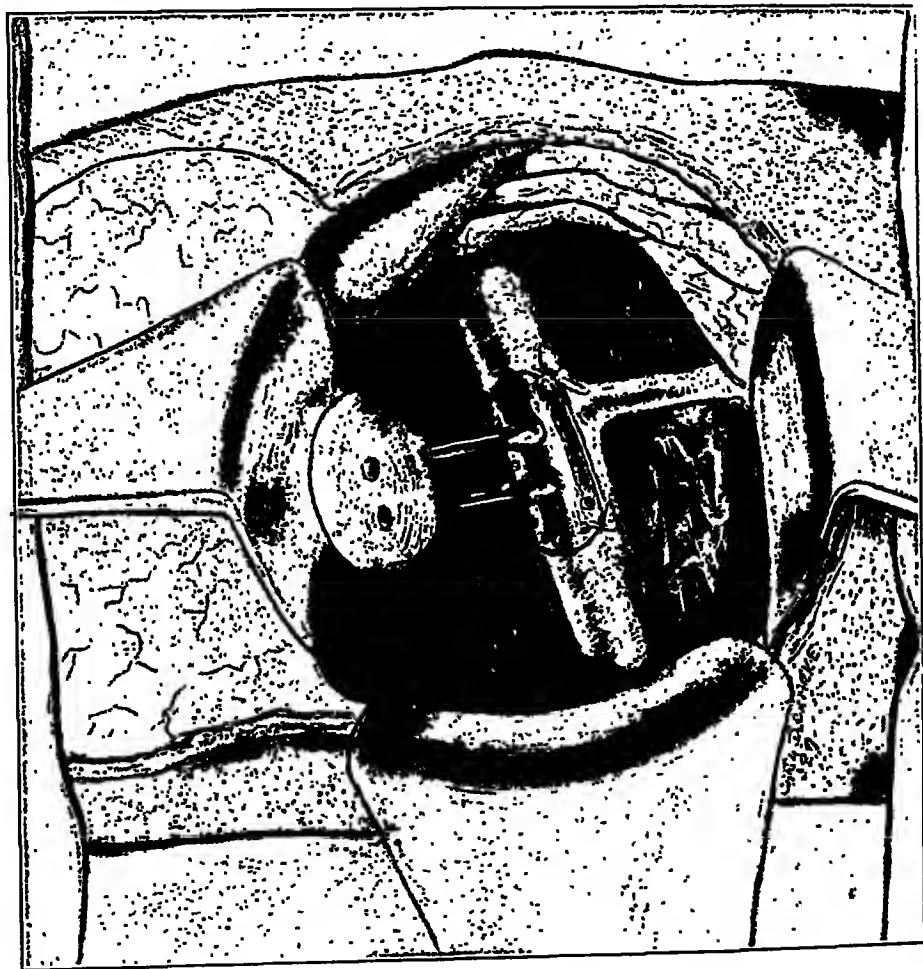


Fig. 5.—Instrument after it is sutured over the vein.

#### ASPIRATION OF THE BLOOD

The round plate of the cannula is grasped between the thumb and index finger. An 18 gage Record needle is passed through the skin into the depressed surface of the plate (A). The needle should be attached to a Record syringe and immediately after it is passed into the cannula, suction should be made with the piston of the syringe. If this technic is used, the portal blood will be aspirated into the syringe on the immediate entrance of the needle into the vein. After the desired quantity of blood is obtained, the needle is withdrawn from the vein, a distance of about one-fourth inch, and a stylet is placed in

the curved plate of the instrument (C) is sutured over the portal vein at the junction of the splenic vein. A curved incision is used to prevent the round plate of the instrument (A) from being placed beneath the scar of the incision. That portion (A) is therefore lateral to the incision. This can be seen in figure 3.

The illustration in figure 4 shows how the instrument is sutured over the portal vein. Four sutures are necessary to hold the instrument in place. It is better to apply all sutures before tying the knots.

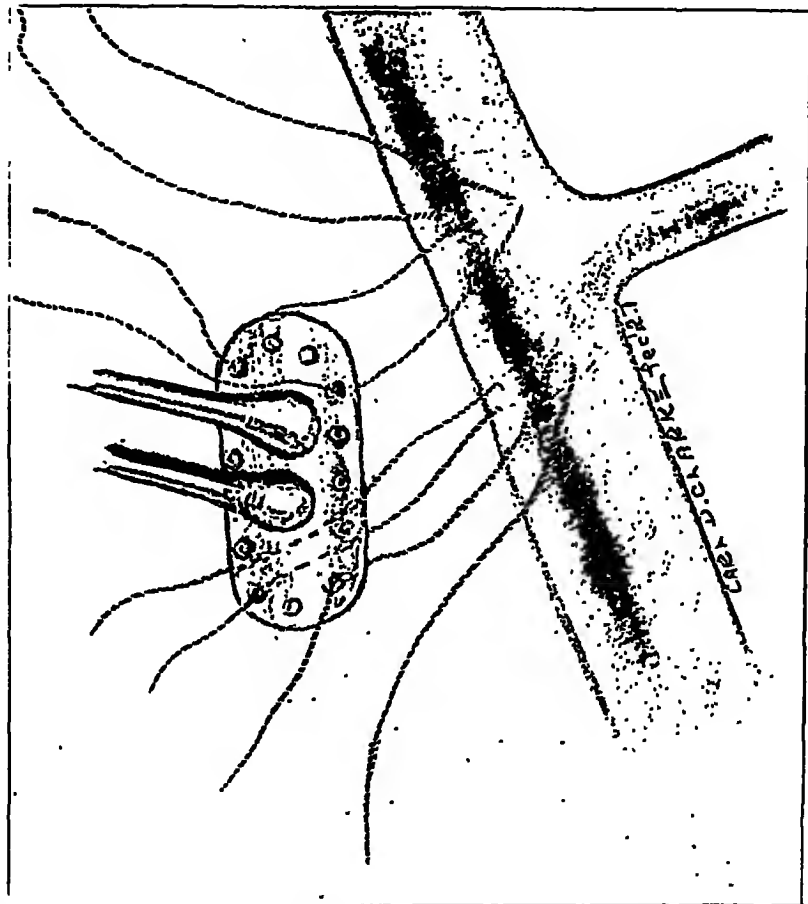


Fig. 4.—Illustration showing how instrument is sutured over the portal vein.

In figure 6 the instrument has been sutured over the vein. This has been done through the incision of the rectus muscle. The semicircular flap incision in the skin, and the plate (A) resting on the lower ribs should be noted.

The plate (A) is brought through the abdominal wall by making a second incision along the costal margin near the lower ribs. This incision includes the muscles and is not made through the skin. The instrument is suspended on the lower ribs to prevent pressure on the vein. The wound in the rectus muscle and peritoneum is closed; catgut is used in the peritoneum and silk in the sheath of the rectus muscle. The semicircular skin incision is sutured with interrupted sutures of silver wire.





Fig. 8.—A dog eighteen months after the introduction of the cannula. Blood may still be aspirated from the portal vein.

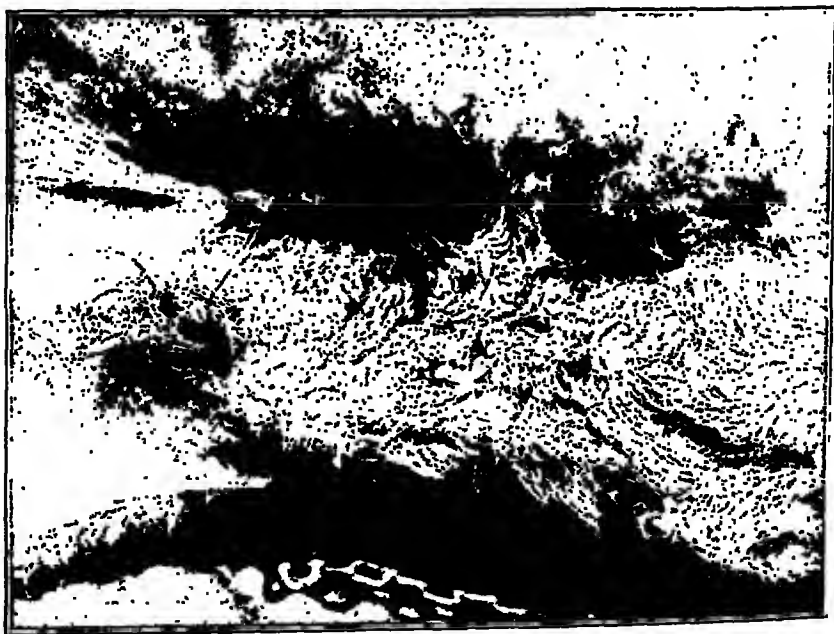


Fig. 9.—Close up view of the abdomen of the dog shown in figure 8. The arrow points to the instrument.

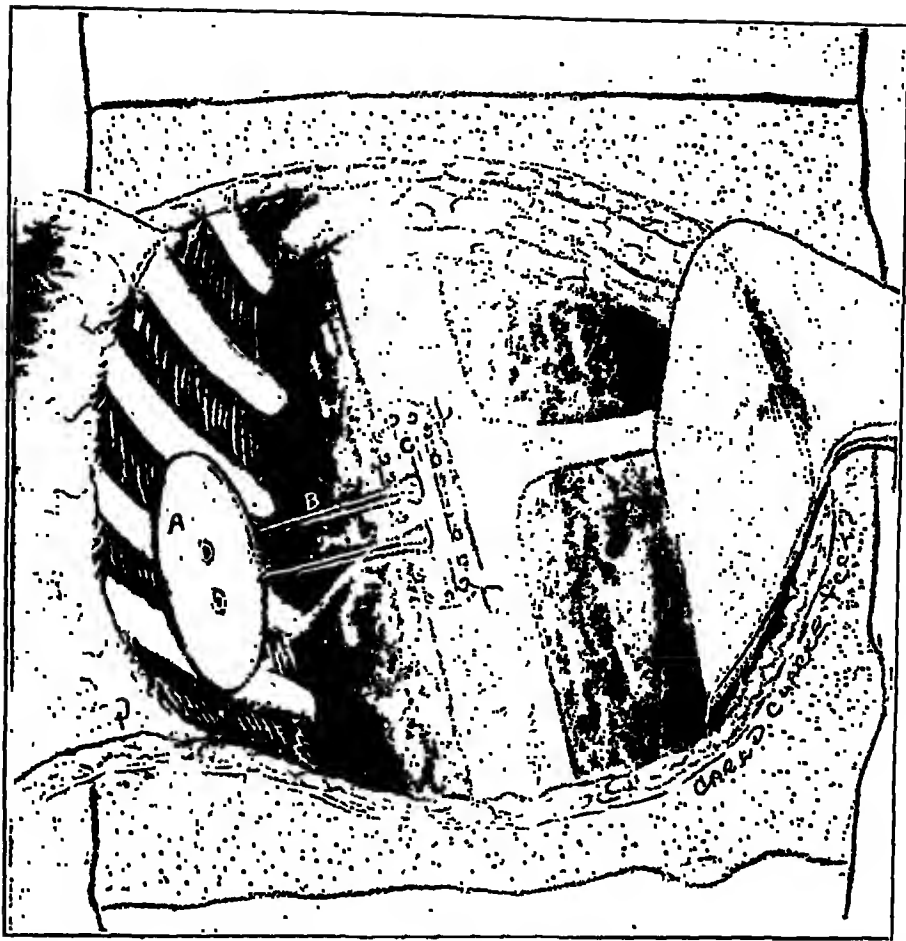


Fig. 6.—Instrument sutured over the vein by means of incision of the rectus muscle.



Fig. 7.—Close up view of the abdomen of the dog shown in figure 3. The scar of the semicircular skin incision and the plate of the instrument beneath the skin, as indicated by the arrow, should be noted.

# TOXIC GOITER AND MENTAL DISEASE

## RELIEF OF PSYCHOSES IN THYROTOXIC PATIENTS BY THYROIDECTOMY \*

JOSEPH L. DECOURCY, M.D.

CINCINNATI

It has long been recognized that disturbances of the thyroid gland may give rise to mental disease, but hitherto attention has been focused largely on ablation of the thyroid function as the principal cause of thyrogenic psychoses. Before thyroid extract was employed, many patients with myxedema were confined in insane asylums. Without treatment, this disease may give rise to so extreme a degree of psychic paralysis that institutional care becomes necessary. Memory is lost, power of volition disappears, and the patient becomes completely indifferent to his surroundings. In cretinism, a somewhat similar train of mental symptoms follows.

The relation between toxic goiter and mental alienation is less generally admitted, yet I have made some observations that have led me to believe that under certain circumstances thyrotoxicosis may be the exciting, or at least a strong contributory, cause of serious mental disease, and that in such cases, particularly when the psychosis is not far advanced, operation may offer a good prospect of mental recovery. During the past five years I have performed thyroidectomy on fourteen frankly insane patients with toxic goiter; all but two recovered sufficiently to resume their former occupations.

### LITERATURE

In 1908, Berkley and Follis<sup>1</sup> reported a study of a series of cases of the catatonic form of dementia praecox, in which they found a definite resemblance between symptoms of exophthalmic goiter and those of catatonia: chiefly, rapid pulse, muscular tremor, hyperhidrosis, over-active eye and other reflexes, rapid loss of weight, disturbance of the menses and vasomotor pareses. They observed that the psychic changes in the prodromal stage of catatonia also resemble those seen in exophthalmic goiter. In most of their cases of catatonia, the thyroid gland was found to be soft and mushy with occasional hard nodules. Usually it was not enlarged. Experiments showed that the administration of iodine, thyroid extract or desiccated thyroid woke the patients out of

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\* From the Department of Surgery, DeCourcy Clinic.

1. Berkley, H. J., and Follis, R.: An Investigation into the Merits of Thyroidectomy and Thyro-Lecithin in the Treatment of Catatonia, *Am. Med.-Psychol. Assoc.* 15:283, 1908.

the needle. This controls hemorrhage from the punctured wound of the vein. The needle is allowed to remain in this position for a few minutes and then may be withdrawn.

Several points should be emphasized in the application of this method besides those already mentioned. Cannulas of various sizes should be made that may be applicable to dogs of different sizes. It would be difficult to use an adjustable instrument. The instrument should be of sufficient length so that there will be neither pressure nor too much tension on the vein. The portal vein in the dog is freely movable, and too much tension by suspension of the instrument on the rib as already described is not likely to occur. If the needle is introduced as described and a stylet placed in the needle after aspirating the blood, hemorrhage will not occur. It is true that the use of a small needle may give rise to some difficulty by the formation of a clot in the needle. If this should occur, the needle may be withdrawn and cleansed or another needle may be used. It is possible that the needle may pass through the portal vein and enter the inferior vena cava. I am now using another separate plate directly over the vena cava, like the plate (C) of the instrument. This plate makes it impossible for the aspirating needle to penetrate the vena cava.

The method has been used successfully in ten dogs. Unlimited aspirations may be made. Figures 8 and 9 show a dog that has retained the instrument for eighteen months. The portal vein in this dog has been aspirated more than fifty times. The dog apparently is normal and has gained weight since the introduction of the cannula. In three of the dogs, the round plate of the cannula ulcerated through the skin in from six to eight months after the introduction of the cannula.

The cannula may be used in the study of absorption from the intestinal tract, in tests on the function of the liver and in the study of the various dyes in tests on the function of the liver by the introduction of these dyes directly into the portal vein.

thyroid gland compatible with the assumption of a thyroid origin of the mental disease. Morse,<sup>4</sup> on the contrary, failed to find any uniform lesions in the thyroid gland in a series of twenty-seven postmortem examinations on patients with dementia praecox.

In 1910, Winslow<sup>5</sup> reviewed the results obtained by Berkley and Follis and by Kanavel and reported five additional cases of dementia praecox in which partial thyroidectomy was performed. One of these patients died with acute thyroidism; two were greatly improved for a considerable period and then relapsed; one was not materially benefited; and one was improved, but could not be kept under observation. From these cases and the results reported by others, Winslow concluded that there seems to be some connection between the thyroid gland and catatonia; that partial thyroidectomy in the early stages of this disease has a favorable, and sometimes a curative, effect; but that, in the late stages, the operation does not have any beneficial results.

In 1922, Weinberg<sup>6</sup> reported eight cases of mental disease with symptoms of hyperthyroidism and somewhat enlarged thyroid glands, but not the typical symptoms of exophthalmic goiter. Two of the patients had the manic-depressive type of psychosis; three, dementia praecox. Thyroidectomy was performed in three cases of this series, including one of the manic-depressive and one of the dementia praecox type, and resulted in complete relief from the mental symptoms.

In 1922, Eastman and Eastman<sup>7</sup> stated:

Since all the clinical symptoms of Graves' disease are largely of nervous origin and all are emotional, many cases exhibiting rather definite forms of nervous and mental disease as mania, chorea, hysteria, etc., it is not at all surprising that the rather definite clinical syndrome of dementia praecox appears occasionally in connection with thyrotoxicosis.

They reported that at the Central Insane Hospital at Indianapolis, 101 consecutive patients with dementia praecox of all types were examined for signs of endocrine imbalance, and especially for thyroid hypertrophy. Of twenty-seven male patients, eleven, or 40 per cent, showed some degree of thyroid enlargement. Two of these patients had large goiters; six, a conspicuous enlargement of the gland; three, moderate hypertrophy of one or both lobes. Of seventy-four female patients, forty-eight, or 64 per cent, showed some thyroid hypertrophy. Eighteen

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4. Morse, M. E.: *Pathologic Anatomy of Ductless Glands in Dementia Praecox*, J. Neurol. & Psychopath. 4:1, 1923.

5. Winslow, R.: *Partial Thyroidectomy in Dementia Praecox*, J. A. M. A. 55:1195 (Oct. 1) 1910.

6. Weinberg, H. M.: *Mental Side of Hyperthyroidism*, Penn. M. J. 25:618, 1922.

7. Eastman, J. R., and Eastman, N.: *Thyroid Surgery and Dementia Praecox Syndrome*, Ann. Surg. 76:438, 1922.

their stupor, so that they became talkative and excited and exhibited increased dermatographia and hyperhidrosis, higher pulse rate and increased tendon reflexes.

A transitory amelioration of the mental symptoms has frequently been observed in cases of dementia praecox following thyroid medication, but lasting benefit has rarely been reported. Wagner-Jauregg,<sup>2</sup> however, noted a favorable influence from treatment with thyroid in some early cases of the hebephrenic type.

Berkeley and Follis performed partial ablation of the thyroid gland in ten cases of catatonia. Four of the patients recovered their mental equilibrium after operation; three improved slowly but progressively without a tendency to relapse. In one of these cases, the pathologic appearance of the thyroid gland was suggestive of exophthalmic goiter. The fourth patient improved rapidly for a time, but relapsed for a few months, during which period the remaining half of the thyroid gland increased in size. When this goiter again decreased in size, the mental condition became normal and remained so. In this case, no pathologic condition other than colloid goiter was found in the portion of the gland that was removed. In another case, there was less improvement but mental deterioration was more advanced, and only a small portion of the gland was removed. In four cases, there was slight fibrosis. Two of the patients were cured by the operation.

Kanavel<sup>3</sup> reported the results of thyroidectomy in eleven cases of dementia praecox, eight of them of the catatonic type. All but two represented cases of from two to ten years' duration. Improvement in the mental condition was not noted after operation. Of the two recent cases of less than one year's duration, one occurred in a patient who had been operated on too recently to judge of the result. The other patient showed definite improvement, but not complete cure. Another case, not included in this series, was noted, in which the thyroid gland was removed because of symptoms of pressure due to enlargement. The operation resulted in marked mental improvement, so that the patient was discharged from institutional care and returned to work. In the eleven cases, ten of the thyroid glands removed were examined pathologically. Only two showed excessive parenchymatous growth; six showed colloid changes. Kanavel noted, however, that colloid glands may result from a degenerative change, and this observation does not absolutely exclude the assumption of a previously perverted excessive thyroidism. Eight of ten patients in this series showed changes in the

2. Wagner-Jauregg: *Organotherapie bei Neurosen und Psychosen*, Wien. klin. Wchnschr. 36:1, 1923.

3. Kanavel, A. B.: *The Advisability of Thyroidectomy in Catatonic Dementia Praecox*, Illinois M. J. 16:253, 1909.

sexes, goiter was most frequently associated with manic-depressive psychosis and dementia praecox. The goiters were chiefly of the adenomatous type; a few, of the colloid type. There were no goiters of the hyperplastic type, and evidence of hyperthyroidism was not present in any case. In a few cases the thyroid was removed, but without effect on the psychosis. In all instances, typical adenomatous changes were found in the removed gland. There were no cases of definite hyperthyroidism. In a study of 800 patients with goiter in a general hospital in the same locality, Foss and Jackson did not find any cases of true insanity. Only two patients showed mild excitement or slight and transient mania. Foss and Jackson, therefore, did not see any definite relationship between goiter and insanity, but they admit that thyroidectomy should be performed when there is evidence of hyperthyroidism in a person with a psychosis.

In 1923, Weiss<sup>11</sup> reported seven cases of psychoneurosis with anxiety states associated with definite symptoms of hyperthyroidism; that is, tachycardia tremor, glittering eyes and moist hands. Partial thyroidectomy in two cases, and roentgen-ray treatment of the thyroid gland in one case, failed to relieve the patient from the psychosis. Weiss believed that the thyrotoxicosis in these cases was not directly responsible for the mental symptoms, but that the two developed concomitantly, both as symptoms of an abnormal degenerative constitution, most probably with disturbance of the vegetative nervous system.

Studies of basal metabolism in dementia praecox indicate that a lowered rate is more frequent than high basal metabolism, which is characteristic of hyperthyroidism. In 1925, in a study of the basal metabolism in 161 cases of mental diseases of various types, Bowman and Fry<sup>12</sup> found that of twenty-four patients with dementia praecox, eighteen showed minus readings, which were abnormally low in seven instances. The manic-depressive group showed a tendency toward low readings in the depressive and hypomanic stages, but this was not so marked as in the cases of dementia praecox. In a review of the literature on basal metabolism in dementia praecox, Bowman and Fry found 125 cases (including their 24 cases). The basal metabolism was high in only eleven of the cases; in fifty-two, it was low, and in fifty-two, normal.

In 1921 and 1922, Lewis and Davies<sup>13</sup> reported a study of twenty-two cases of dementia praecox in which the thyroid feeding test was

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11. Weiss, R. F.: Psychoneurotische Störungen bei Hyperthyroidismus, *Ztschr. f. klin. Med.* 97:366, 1923.

12. Bowman, K. M., and Fry, C. C.: Basal Metabolism in Mental Disease, *Arch. Neurol. & Psychiat.* 14:819 (Dec.) 1925.

13. Lewis, N. D. C., and Davies, G. R.: Correlative Study of Endocrine Imbalance and Mental Diseases, *J. Nerv. & Ment. Dis.* 54:385, 493, 1921; 55:13, 1922.

of these had actual goiters, nine of which were apparently cystic. In both male and female patients, however, "the cardinal symptoms of thyrotoxicosis, except goiter, were notably absent." Eastman and Eastman reported four cases, all in females with the paranoid type of dementia praecox, in which one lobe of the thyroid or one lobe with the isthmus was enlarged. Two of the patients showed slight exophthalmos; the other two did not show any ocular signs of exophthalmic goiter. There were no frank symptoms of thyrotoxicosis, but all patients showed accelerated pulse rate and some tremor of the fingers. A hemithyroidectomy was performed in the four cases and in all the psychosis was entirely relieved, the patients returning to their usual occupations.

In 1924, Jackson<sup>8</sup> reported a psychosis in a woman, aged 53, who had typical symptoms of exophthalmic goiter, although exophthalmos was slight. The thyroid gland was symmetrically enlarged to a slight degree. It felt firm and fibrous, being a typical hyperplastic gland. The right superior thyroid artery was first ligated. This operation resulted in a severe reaction with exacerbation of all the symptoms. Ligation of the left superior thyroid artery, however, resulted in marked improvement. Later, two thirds of the right lobe and isthmus were resected. Two weeks after this operation the basal metabolic rate fell to normal, and the patient was mentally normal.

In 1926, Boys<sup>9</sup> stated that in his series of cases of toxic goiter he found that about 2 per cent show mental symptoms so severe that they may be called definite psychoses. He reported eight cases in which there were well developed mental symptoms and goiter. In six of these cases, removal of the thyroid gland resulted in complete recovery. The thyroid glands were grossly or microscopically hyperplastic, and the symptoms of hyperthyroidism had preceded the development of the psychosis. In one case there was an adenomatous goiter without hyperplasia, and in another, a simple colloid goiter. In neither of the cases were the mental symptoms improved by operation, nor had the symptoms of goiter preceded the development of the psychosis. One of the patients relieved by thyroidectomy was affected with the manic-depressive type of psychosis.

In 1924, Foss and Jackson<sup>10</sup> reported an incidence of 59 cases of goiter among 1,647 patients at the State Hospital in Danville, Pa. As this institution is in a goiter belt, this is not a high incidence of goiter. Forty-nine of the goiters were in women; ten in men. In both

8. Jackson, A. S.: Value of Ligation in Psychosis of Exophthalmic Goiter, *Wisconsin M. J.* 22:426, 1924.

9. Boys, C. E.: Psychoses Associated with Goitre, *J. Michigan M. Soc.* 25: 653, 1926.

10. Foss, H. L., and Jackson, J. A.: Relationship of Goiter to Mental Disorders, *Am. J. M. Sc.* 167:724, 1924.



sanitarium in one of the suburbs, where she remained for a month. There was great physical improvement during this period; the weight increased and the pulse rate came down to normal.

She was then taken to her sister's home in Cincinnati, and immediately her mental condition began to become clear. Three months after the operation, her mind appeared entirely normal. The following month, she took a motor trip East by herself without suffering any mishap. She has been under observation for a year since that time and is now entirely well. Judging by her present condition, there is every reason to believe that she will remain so.

It would seem that in this case the mental disturbance belonged to the group of exhaustion psychoses. Apparently thyroidectomy, by removing the source of toxemia, was the essential factor in restoring mental balance.

CASE 2.—A white woman, aged 30, married, exhibited a mental disturbance characterized by a marked paranoid trend. For four years she had noticed a fulness in her neck. During the past year this growth had increased in size and she had become emotional and irritable. Since the birth of her last child fourteen months previously, she had lost 20 pounds (9 Kg.)

During the last three months the nervous symptoms had increased perceptibly, and her husband reported that at times her conduct was unusual. On one occasion she left home and was found late at night wandering in a nearby wood. She had loose, poorly organized delusions of persecution, such as are commonly observed in the paranoid type of dementia praecox. She believed that everybody was against her and feared that her husband was trying to kill her with poison. For this reason she refused to take medicine. The family history was negative with regard to mental disease and goiter.

On examination the patient appeared well developed but considerably below normal weight. She looked excited and apprehensive. Her appearance was typical of thyrotoxicosis. Her temperature was 99 F.; her pulse rate, from 130 to 140. The thyroid gland was about three times the normal size and of the consistency of a hyperplastic goiter.

After the usual preparation with a compound solution of iodine, thyroidectomy was performed. After one week she was taken home. Physical improvement was marked, but the mental derangement became worse. After about three months of treatment, however, during which time she ran away from home twice and frequently became so excited that hypnotics were required, she began to improve slowly. This improvement continued over a period of a year, at the end of which her mental status seemed normal. Eighteen months after operation, she was entirely well and her mental condition was clear.

The mental disturbance at the onset of the illness would suggest dementia praecox. In two other cases this diagnosis had actually been made and a poor prognosis given; yet both patients recovered completely after thyroidectomy.

#### SUMMARY

With the exception of the thyrogenic psychoses occasionally associated with myxedema and cretinism, it is generally held that a direct relationship does not exist between the thyroid gland and mental disease. Careful examination of the thyroid gland in cases of dementia praecox and other psychoses has failed to reveal any consistent anatomic changes.

performed. Evidence of hyperthyroidism was found in four cases. One of the patients showed definite symptoms of exophthalmic goiter. Thyroidectomy was performed in this case; but a change in the mental condition did not result, although physical symptoms were relieved. Two of the other patients with hyperthyroidism were fed with suprarenal gland; one, with suprarenal and pituitary gland. One of the patients showed marked improvement with regard to mental symptoms and was discharged as recovered. In twelve cases of this series there was definite evidence of hypothyroidism. The thyroid feeding test was found to be of definite value in distinguishing between cases of hyperthyroidism and hypothyroidism.

#### RESULTS

During the past five years, I have operated on fourteen mentally unbalanced patients with toxic goiter. The mental symptoms were extremely pronounced in the majority of cases, yet all but two patients recovered completely and were able to resume their former occupations. They have remained clear mentally to date.

In two instances, both in young persons, a diagnosis of dementia praecox was made and a poor prognosis given; yet both patients recovered. In all but one case, the derangement occurred in persons suffering from the exophthalmic type of goiter. The exception was a case of the toxic adenomatous type, also with evidence of hyperplasia.

The period during which mental recovery took place varied from several months to a year. Two patients with dementia were not improved by operation; one died in an asylum, the other is still an inmate. In one case, a psychosis developed on the eighth day following removal of an extremely toxic goiter, and this patient is still in a sanitarium.

#### REPORT OF CASES

CASE 1.—A white woman, aged 35, single, was first seen at the Connecticut State Insane Asylum, Middletown, Conn., when she was in a highly excited state and could not orient herself as to time or place. During the preceding six months, she had lost 40 pounds (18.1 Kg.).

Examination revealed an enlarged thyroid gland, of the consistency found in hyperplastic goiter, with an adenoma about the size of an egg overlying the right lobe. Tremor was pronounced. The pulse rate varied between 140 and 160 and was weak.

The patient was removed to the Good Samaritan Hospital, Cincinnati, being accompanied on the trip by her sister and a nurse. During the journey she made several attempts to leave the train and was continually muttering unintelligibly. While in the hospital at Cincinnati, she tried several times to eat her own feces.

With rest and the administration of a compound solution of iodine she began to improve physically, but her mental condition remained the same. Two weeks after her arrival, thyroidectomy was performed. The reaction was slight and the postoperative course uneventful. Following operation, she was removed to a

# VITAL CAPACITY

## ITS SIGNIFICANCE IN RELATION TO POSTOPERATIVE PULMONARY COMPLICATIONS \*

JOHN H. POWERS, M.D.

BOSTON

Determinations of vital capacity, heretofore utilized chiefly by physiologists or restricted to the study of serious cardiac or pulmonary disabilities, are now finding a wider application. The ease with which this accurate information is accumulated has greatly facilitated the dissemination of its practical value.

The determination of the vital capacity of any given patient is clearly one method of appraising the condition present. Any disorder which affects the cardiovascular or respiratory systems reduces the vital capacity. Such determinations may be of use not only in the diagnosis of these cardiorespiratory afflictions, but they also may be of assistance in determining the fitness of any given person. This may be utilized in surgical procedures to appraise the ability of a patient to withstand an operation. Since so many operations of today are those of election, the acquisition of this information seems desirable. Accurate knowledge of pulmonary and cardiac reserve energy might prove to be of inestimable value in deciding on the operability of patients before subjecting them to prolonged procedures. It would seem especially applicable to elderly or debilitated patients and to those whose past history reveals evidence of previous cardiac or pulmonary pathologic conditions. Already articles have appeared relative to the effect of certain surgical conditions and different types of operative incisions on the vital capacity. These latter studies are of great importance since they give a rough estimate of the reduction that follows certain incisions, the position of which interferes with free respiration. Such studies create normal base lines below which further reductions have a deeper significance.

The startling increase in the number of postoperative pulmonary complications during the past two decades points to the importance of making accurate observations during the convalescent period. Pfannenstiel,<sup>1</sup> in 1903, and Otte,<sup>2</sup> in 1907, reported large series of cases in which postoperative pulmonary complications were not observed, a

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\* From the Surgical Clinic of the Lakeside Hospital, Cleveland.

1. Pfannenstiel, J.: Ueber die Vorzüge der Äthernarkose, *Zentralbl. f. Gynäk.* 1:8, 1903.

2. Otte, A.: Ueber die postoperativen Lungenkomplikationen und Thrombosen nach Aethernarkosen, *München. med. Wchnschr.* 54:2473, 1907.

However, toxic goiter is sometimes observed in association with serious mental diseases, and experience has proved that in such cases, not only the physical condition, but the psychosis as well, may be benefited materially by thyroidectomy. When the mental disturbance is of recent onset and the thyrotoxic manifestations are severe, a fair prospect of mental recovery may be offered following thyroidectomy.

My experience in the treatment for combined toxic goiter and mental alienation comprises fourteen cases, in which I performed thyroidectomy during the past five years. Although the mental symptoms were extremely pronounced in the majority of these cases, all but two of the patients recovered mentally and were able to resume their former occupations, remaining normal to date. In two of the cases, the diagnosis of dementia praecox had been made and a poor prognosis given, yet both patients recovered. In all but one instance, the goiter was of the exophthalmic type; the exception was a toxic adenomatous goiter with evidence of hyperplasia. When thyroidectomy is performed on patients with psychoses, preoperative rest, medication with a compound solution of iodine and the most perfect operative technic are perhaps even more important than in patients with normal mentality.

dence of a pathologic process in the chest could well have escaped recognition.

Even such an extensive lesion as massive atelectasis of one lung passed unrecognized for many years by physicians and surgeons alike. The condition was first described by Pasteur<sup>11</sup> in 1908, but the first cases of postoperative collapse to be reported in the American literature did not appear until 1921.<sup>12</sup>

These studies on the vital capacity of surgical patients were undertaken with the hope of establishing a means of detecting transient, minor postoperative upsets and corroborating the diagnosis of gross pulmonary complications.

#### METHOD

Dr. Francis Peabody<sup>13</sup> stated:

"The vital capacity of the lungs consists of the volume of the deepest possible expiration after the greatest possible inspiration. A certain amount of air, known as the residual air, remains in the lungs after complete expiration but the vital capacity represents the degree of movability of the lungs and anything which interferes with the movement of the lungs, preventing the entrance of the air into them, causes a decrease in the vital capacity."

Any acute process in the abdomen producing reflex spasm of the abdominal musculature involves the accessory muscles of respiration and hence inhibits respiratory excursion. Likewise, any operative procedure attended subsequently by splinting of the abdomen has a direct influence on the vital capacity. Consequently, it was necessary first to establish normal curves in order to determine the reduction in vital capacity following the various types of operative procedures in uncomplicated cases.

All the male patients admitted to the surgical service of the Lakeside Hospital were studied during a period of several months. At first the female patients were included, but the men were found to be more cooperative and the results accordingly more satisfactory. All the patients were encouraged to exert themselves to the utmost in spite of pain, and a friendly spirit of rivalry was stimulated in the ward, each man trying to "blow harder" than his neighbor in the next bed. Whenever it was felt that a patient was not cooperating fully, his observations were discarded.

The Collins Vital Capacity Spirometer was used. It consists of a delicately compensated bell floating in a cylinder of water. The most essential feature of the apparatus is the direct reading dial which is graduated to tenths of liters. Fractions of these graduations may be estimated in tenths also. As the bell rises with expiration, a movable pointer passes over the face of the dial, stops at the highest point and remains in that position. A second pointer is connected with the dial which is of value if the patient tends to inspire from the spirometer just before expiring into it. In such a case, the bell may be raised and the pointers adjusted so that both are at the 1 liter mark. If the

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11. Pasteur, W.: Massive Collapse of the Lung, *Lancet* 2:1351, 1908.

12. Scrimger, F. A. C.: Postoperative Massive Collapse of the Lung, *Surg. Gynec. Obst.* 32:486, 1921.

13. Peabody, F. W.: The Clinical Importance of the Vital Capacity of the Lungs, *Northwest Med.* 22:307, 1923.

remarkable and praiseworthy record. In the light of present knowledge, however, it is possible that a reexamination of the individual case reports might reveal minor symptoms indicative of transient pulmonary complications.

In 1906, Armstrong<sup>3</sup> reported a pulmonary morbidity of 2.12 per cent in 2,500 cases at the Montreal General Hospital. In 1908, von Lichtenberg<sup>4</sup> collected 23,673 cases with a pulmonary morbidity of 1.9 per cent. The same year, Ranzi<sup>5</sup> published 263 pulmonary complications from 6,871 operations in von Eiselberg's Clinic at Vienna, a morbidity of 3.8 per cent. Beckman<sup>6</sup> reported the pulmonary complications at the Mayo Clinic in 1910, 1912 and 1913. When his figures are amended to include pulmonary embolism, they reveal morbidities of 1.12 per cent, 1.57 per cent and 1.27 per cent, respectively. Cutler and Morton<sup>7</sup> found 1.86 per cent of cases in 3,490 operations at the Massachusetts General Hospital in 1917. One year later, McKesson<sup>8</sup> computed 3.03 per cent of pulmonary complications from the combined statistics of 39,438 operations. In 1920, Cutler and Hunt<sup>9</sup> reported a pulmonary morbidity of 3.52 per cent in 1,562 patients operated on at the Peter Bent Brigham Hospital, and the following year,<sup>10</sup> 3.92 per cent in 1,604 cases at the same hospital.

It seems probable that a more careful analysis of all these statistics would reveal not actually a greater number of postoperative complications during recent years, but a more astute recognition and correct interpretation of symptoms which heretofore have passed unnoticed. A slight unexplained fever, a transient cough with or without thoracic pain, a few flecks of blood-tinged sputum without gross clinical evi-

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3. Armstrong, G. E.: Lung Complications After Operations with Anesthesia, *Brit. M. J.* 1:1141, 1906.

4. Von Lichtenberg, A.: Die postoperativen Lungenkomplikationen, *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.* 11:129, 1908.

5. Ranzi, E.: Ueber postoperative Lungencomplicationen embolischer Natur, *Arch. f. klin. Chir.* 87:380, 1908.

6. Beckman, E. H.: Pulmonary and Circulatory Complications Following Surgical Operations, *Collected Papers Mayo Clinic, Philadelphia, W. B. Saunders Company, 1910, pp. 594-599; Complications Following Surgical Operations, ibid., 1912, pp. 738-745; Complications Following Surgical Operations, ibid., 1913, pp. 776-788.*

7. Cutler, E. C., and Morton, J. J.: Postoperative Pulmonary Complications, *Surg. Gynec. Obst.* 25:621, 1917.

8. McKesson, E. I.: Some Observations on Postoperative Lung Complications, *Am. J. S. (Anes. Supp.)* 32:16, 1918.

9. Cutler, E. C., and Hunt, A. M.: Postoperative Pulmonary Complications, *Arch. Surg.* 1:114 (July) 1920.

10. Cutler, E. C., and Hunt, A. M.: Postoperative Pulmonary Complications, *Arch. Int. Med.* 29:449 (April) 1922.

Chart 4 represents the average vital capacity and temperature of five patients who were subjected to upper abdominal operations. Table 4 presents the daily readings in detail. The third patient in the series had a perforated gastric ulcer. On admission, there was marked

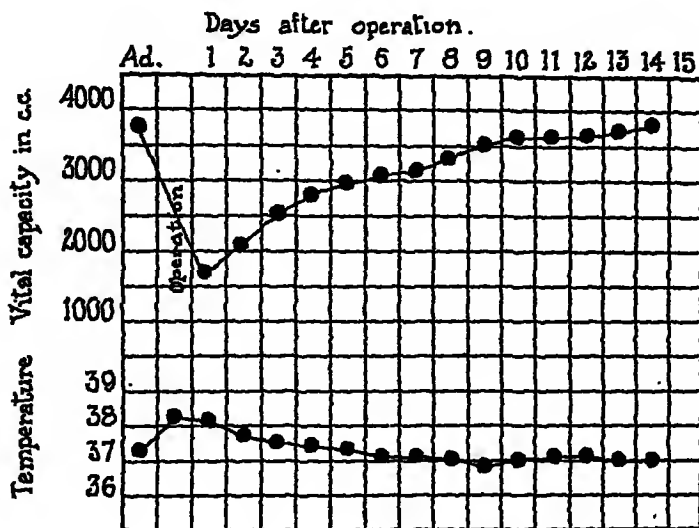


Chart 1.—Composite curve showing the vital capacity of eight patients who were operated on for bilateral inguinal hernia.

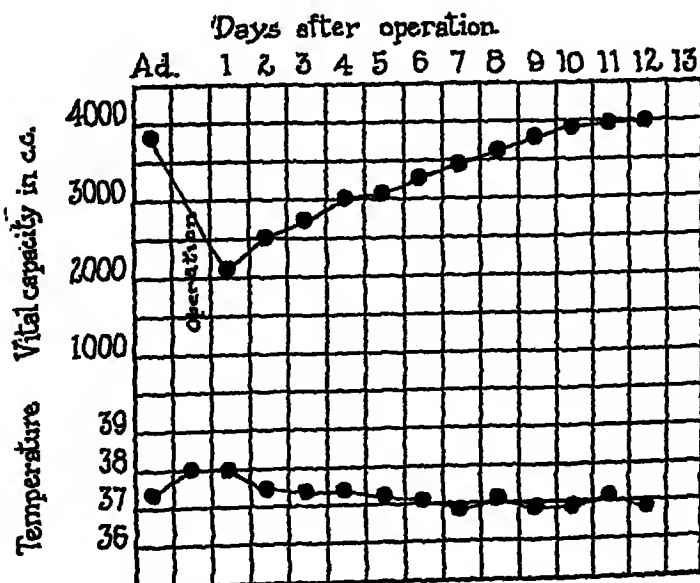


Chart 2.—Curve showing the vital capacity and temperature in eight uncomplicated cases in which operation for unilateral inguinal hernia was performed.

spasm of the whole abdomen and likewise a striking decrease in the vital capacity, 1,800 cc. compared with 5,420 cc. on the fifteenth post-operative day.

patient inspires from the apparatus before expiring, one pointer moves toward the zero mark until inspiration ceases. The other moves in a clockwise direction with expiration. In this case, the difference between the two pointers represents the vital capacity of the lungs. The calibration of the apparatus is exact and the breathing tube is sufficiently large to prevent resistance to expiration.

A nose clip was not used; the patient was instructed to close his nose by gentle pressure of the thumb and finger. Whenever leakage occurred, it could be easily detected by fogging on the polished metal surface of the mouthpiece.

All observations were made with the patients in the recumbent position and are accordingly slightly lower than the average recorded for patients of equal height and weight in the erect posture.<sup>14</sup> They were also taken at least two hours after a meal in order to obviate the possible inhibitory effect of abdominal distention.

The vital capacity was taken on admission and daily throughout the post-operative convalescent period, until a high level was reached or the patient discharged.

The highest of three to five observations was chosen as the most accurate. A record was kept of the operative procedure, the type and the duration of the anesthetic. There were no untoward wound results, even in patients with several drains in the abdomen. Clean wounds healed firmly by primary union as usual. A careful clinical record was kept throughout the patient's sojourn in the hospital and correlated with the vital capacity each day. As an index of the patient's general condition the temperature curve has been plotted beneath the vital capacity.

#### OBSERVATIONS ON NORMAL PATIENTS

All the similar types of cases have been grouped together. The preoperative level in each has been arbitrarily regarded as 100 per cent and the daily reductions calculated in percentages of this figure.

Chart 1 represents the composite curve of eight uncomplicated operations for bilateral inguinal hernia. Table 1 gives the daily readings for each patient in detail with the average and percentage calculated below.

Chart 2 is a record of the vital capacity and temperature in eight uncomplicated operations for unilateral inguinal hernia. Table 2 is a detailed representation of the daily readings for each patient with the average and percentage calculated below.

Chart 3 and table 3 are representative of eight patients operated on through a McBurney incision for acute appendicitis. The higher readings during the latter days of the convalescence indicate a diminished vital capacity on admission. This was undoubtedly caused by the limitation of respiratory excursion incidental to an acute process in the abdomen.

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14. Christie, C. D., and Beams, A. J.: The Estimation of Normal Vital Capacity, *Arch. Int. Med.* 30:34 (July) 1922.



of fingers and toes, incision and drainage of osteomyelitis, incision, drainage and arthrodesis of joints.

Some interesting results were obtained in patients subjected to thyroidectomy. Chart 9 shows an immediate and striking reduction in

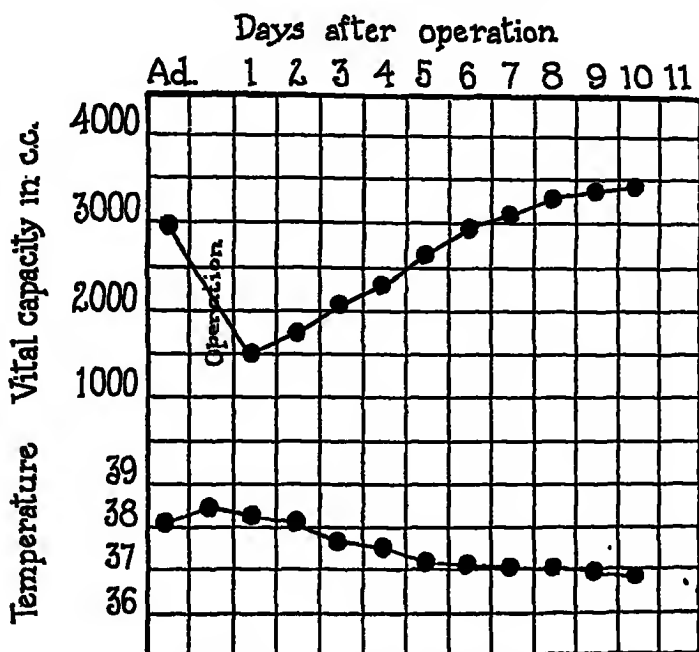


Chart 3.—Vital capacity of eight patients on whom appendicectomy was performed (McBurney).

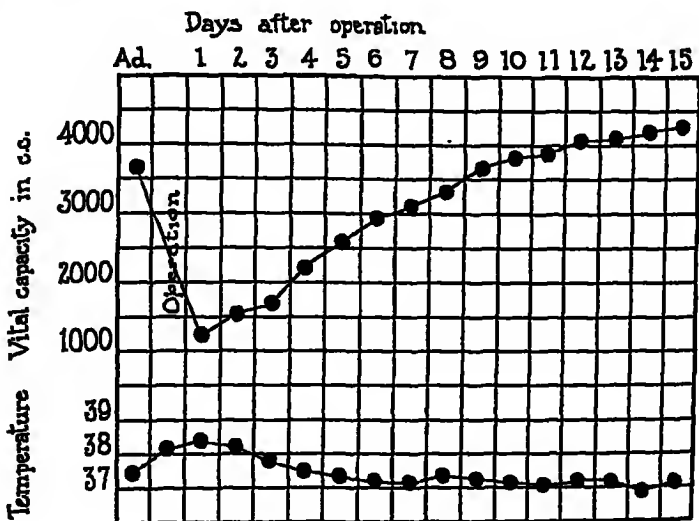


Chart 4.—Average vital capacity and temperature of five patients who were subjected to operation on the upper part of the abdomen.

vital capacity followed by a rapid recovery. Table 8 is a detailed analysis of each case.

Other operations on the neck have only a slight effect on the vital capacity. This lies within the limits of normal daily variation and

There was only one uncomplicated operation involving a midline incision in the lower part of the abdomen. Resection of the bladder and transplantation of the ureters into the rectum were performed for carcinoma of the bladder. This curve is presented in chart 5.

Seven patients were operated on for hydrocele. A slight reduction in the vital capacity occurred during the first few days after operation, in spite of the fact that the aponeurosis of the external oblique was not

TABLE 1.—*Vital Capacity of Patients Operated On for Bilateral Inguinal Hernia Given in Cubic Centimeters*

On Admis- sion	Days After Operation													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3,560	2,250	2,600	2,950	2,990	3,050	3,220	3,150	3,000	3,250	3,200	3,550	3,700	3,660	3,700
3,300	1,720	2,200	2,580	2,310	2,630	2,720	2,000	3,020	3,150	3,100	3,400	3,500	3,410	3,520
5,000	2,440	2,700	3,800	4,200	4,320	4,450	3,900	4,450	4,800	5,050	4,150	3,900	4,500	4,550
2,350	1,900	1,980	2,100	2,500	2,530	2,600	2,730	2,740	2,720	2,800	2,810	2,920	2,930	2,930
3,500	1,000	1,000	1,320	1,740	1,800	2,120	2,680	2,920	3,000	3,180	3,400	3,500	3,500	3,500
3,900	1,000	1,780	1,810	2,600	2,720	2,700	2,800	3,100	3,530	3,750	3,550	3,600	3,600	3,910
3,880	1,700	1,820	2,140	2,310	2,510	2,700	3,120	3,200	3,350	3,350	3,850	3,800	3,510	3,610
4,600	1,550	2,950	3,500	3,700	3,810	4,010	4,060	4,300	4,100	4,430	4,600	4,600	4,700	4,750
3,761	1,635	2,141	2,525	2,803	2,921	3,077	3,167	3,350	3,506	3,629	3,606	3,627	3,734	3,846
100%	45%	57%	67%	74%	77%	81%	81%	89%	92%	95%	95%	96%	99%	102%

TABLE 2.—*Unilateral Inguinal Hernia*

On Admis- sion	Days After Operation											
	1	2	3	4	5	6	7	8	9	10	11	12
3,800	1,740	1,950	2,210	2,510	3,190	3,300	3,420	3,680	3,900	3,850	3,900	3,910
3,900	3,570	3,400	3,310	3,410	3,610	3,900	3,930	4,110	4,190	4,270	4,200	4,200
3,690	2,050	2,300	2,710	3,070	3,220	3,520	3,500	3,600	3,600	3,710	3,770	3,820
3,550	1,830	2,740	2,990	3,240	3,140	3,450	3,570	3,670	3,700	3,750	3,760	3,760
3,000	1,700	2,150	2,590	2,640	2,710	2,800	3,000	2,960	3,200	3,250	3,300	3,600
5,300	2,840	3,320	3,320	3,710	3,700	4,000	4,300	4,790	4,900	5,220	5,300	5,190
3,800	2,500	2,800	3,300	3,350	2,820	3,320	3,400	3,480	3,690	3,820	3,870	3,830
3,980	1,640	2,040	2,400	2,400	2,550	2,450	3,000	3,200	3,620	3,880	3,820	3,900
3,250	1,630	1,820	2,100	2,380	2,630	2,910	3,100	3,120	3,320	3,300	3,400	3,400
3,608	2,188	2,505	2,709	3,000	3,090	3,319	3,489	3,630	3,791	3,902	3,924	3,991
100%	57%	65%	72%	78%	81%	87%	91%	95%	99%	102%	103%	104%

incised. Curves are represented in chart 6 and daily readings are given in detail in table 5.

Rectal operations, including hemorrhoidectomies, excision of fistulas, incision and drainage of ischiorectal abscesses, do not produce any postoperative reduction in vital capacity. Chart 7 is a composite curve of the vital capacity and temperature of eight patients. Table 6 presents the daily observations in detail.

Operations on the extremities likewise do not have any appreciable effect on the vital capacity other than that which can be explained on the basis of daily variation; (chart 8, table 7). Fifteen patients were studied. The operations include excision of varicose veins, amputations

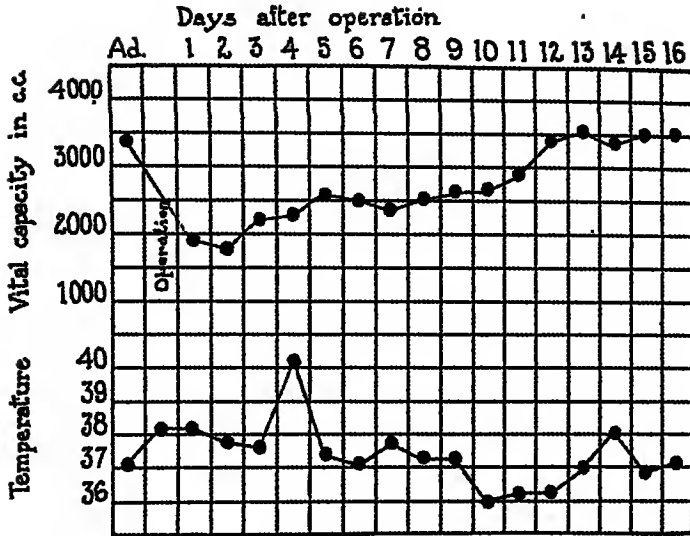


Chart 5.—Vital capacity of one patient following resection of the bladder and transplantation of the ureters.

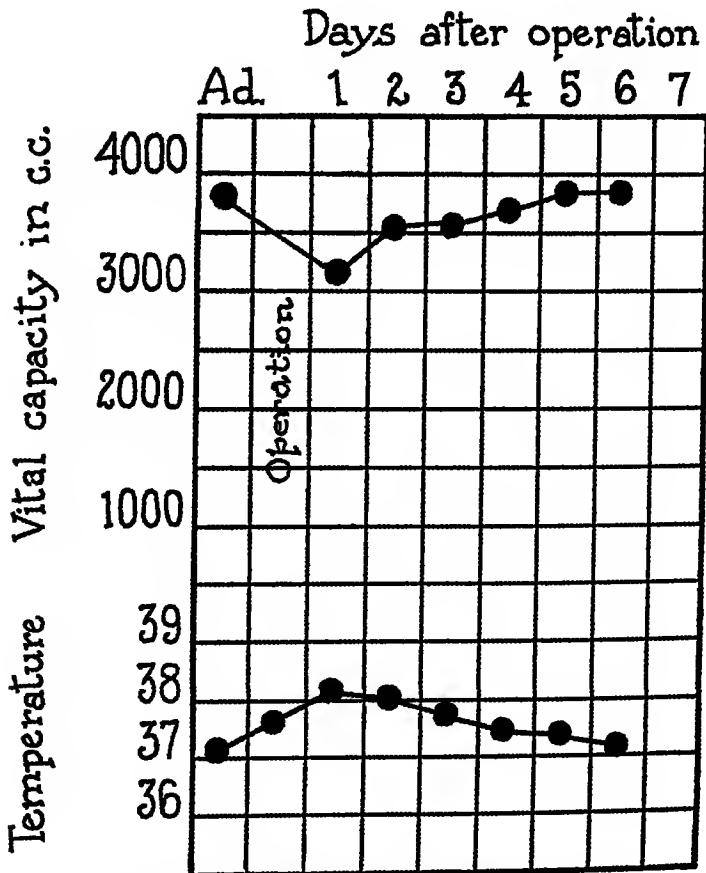


Chart 6.—Vital capacity of seven patients operated on for hydrocele.

probably has no bearing on the operative procedure. The four cases include excision of tuberculous glands, incision and drainage of an abscess, and radical dissection (chart 10, table 9).

#### OBSERVATIONS ON PATIENTS WITH POSTOPERATIVE COMPLICATIONS

There were no complications among the patients operated on for bilateral inguinal hernia.

Chart 11 is a graph of the vital capacity and temperature of a healthy man, aged 26, who was operated on for right inguinal hernia under gas-oxygen-ether anesthesia. The usual reduction in vital

TABLE 3.—*Acute Appendicitis (McBurney Incision)*

On Admis- sion	Days After Operation									
	1	2	3	4	5	6	7	8	9	10
2,540	1,420	1,350	1,550	1,910	2,100	2,500	2,660	2,820	2,820	2,800
1,820	1,410	1,460	1,590	1,720	1,900	2,100	2,400	2,800	2,910	2,910
3,120	1,360	1,400	1,580	1,700	2,100	2,350	3,000	2,850	3,160	3,150
4,050	1,550	1,840	2,310	2,600	3,080	3,480	3,610	3,820	4,060	4,260
3,480	1,680	1,940	2,090	2,850	3,430	3,610	3,780	4,080	4,100	4,100
3,000	2,060	2,580	2,970	3,310	3,510	3,680	3,830	3,950	3,950	3,900
2,110	1,710	1,900	1,980	2,040	2,300	2,340	2,600	2,450	2,600	2,600
3,100	1,080	2,080	2,490	2,910	3,150	3,510	3,510	3,710	3,700	3,710
2,977	1,534	1,819	2,108	2,220	2,696	2,944	3,184	3,304	3,413	3,436
100%	52%	61%	70%	78%	90%	93%	106%	110%	114%	115%

TABLE 4.—*Operations on the Upper Part of the Abdomen*

On Admis- sion	Days After Operation														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
3,680	900	1,300	1,100	1,760	2,800	3,000	2,850	3,390	3,750	3,650	3,700	3,750	3,750	3,750	3,750
3,830	1,090	1,950	2,450	2,760	2,720	2,880	3,000	3,230	3,500	3,450	3,500	3,760	3,520	3,900	3,900
1,900	1,350	2,460	2,840	3,410	3,720	4,450	5,180	4,950	5,210	5,370	5,880	5,420	5,420	5,410	5,420
3,380	1,050	980	1,300	1,640	1,760	2,080	2,200	2,500	2,790	2,950	2,980	3,050	3,210	3,320	3,300
5,430	1,250	1,060	950	1,760	2,150	2,230	2,720	2,820	3,180	3,690	3,820	4,350	4,520	4,730	5,100
3,624	1,248	1,550	1,724	2,266	2,530	2,924	3,180	3,384	3,682	3,802	3,876	4,066	4,084	4,222	4,204
100%	34%	43%	48%	63%	70%	81%	88%	93%	101%	103%	107%	112%	112%	116%	118%

capacity occurred on the first postoperative day. When the observations were taken on the forenoon of the second day a marked secondary reduction was found. During the early afternoon, the patient developed acute respiratory distress; temperature, pulse and respirations were elevated, and physical examination of the chest revealed a massive atelectasis on the right side. This was confirmed by a roentgenogram. On the third day, a slight increase in vital capacity and fall in temperature were observed. On the fourth day, the vital capacity was again reduced and the temperature elevated. Following this, both rapidly returned to normal (compare with chart 2).

Chart 12 is most interesting. The patient was a well developed, but somewhat plethoric man, aged 44, who had suffered with chronic asthma

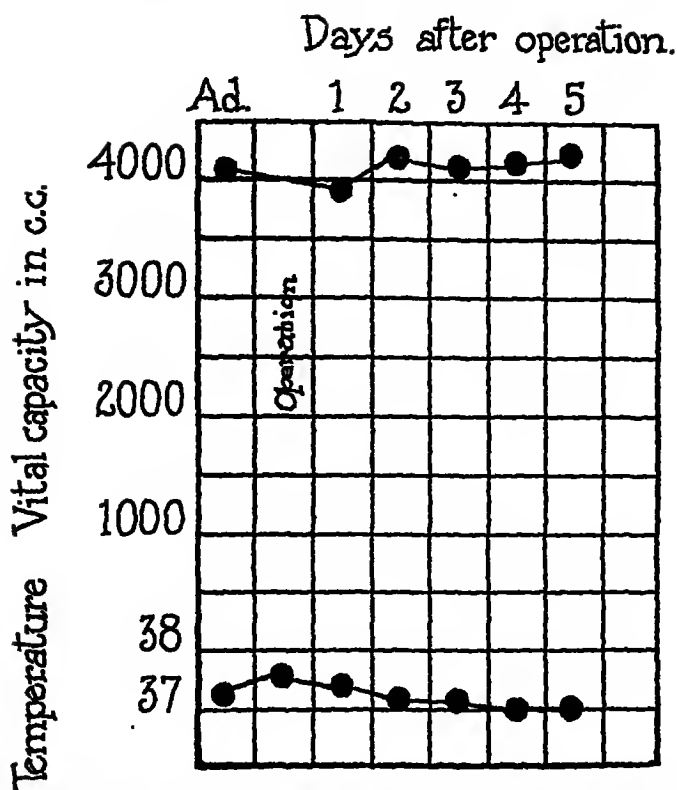


Chart 7.—Composite curve of the vital capacity and temperature of eight patients on whom rectal operations were performed.

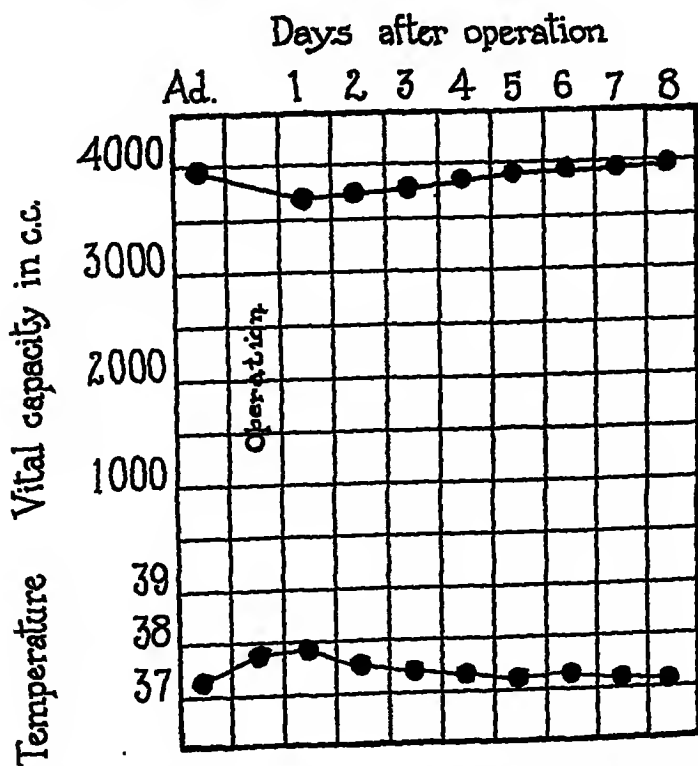


Chart 8.—Vital capacity of fifteen patients who were subjected to operations on the extremities.

for many years. Examination of the chest revealed typical asthmatic symptoms; clubbing of the fingers and toes was present. The pre-operative vital capacity was only 2,650 cc., 64 per cent of the expected normal for a man of corresponding height and weight. A right inguinal hernia was repaired under local infiltration and block anesthesia with procaine hydrochloride. The usual reduction in vital capacity occurred on the first postoperative day, accompanied by a marked elevation in temperature. During the subsequent four days, the vital capacity increased slowly, but the temperature remained elevated. On the sixth day, a decrease in vital capacity was noted. During the next three

TABLE 5.—*Hydrocele*

On Admission	Days After Operation					
	1	2	3	4	5	6
4,660	4,100	4,160	4,200	4,680	4,680	4,660
3,610	3,170	3,290	3,140	3,800	3,850	3,550
3,800	2,500	2,700	2,930	3,200	3,510	3,510
3,470	3,140	3,500	3,550	3,550	3,550	3,550
4,500	4,200	4,700	4,520	4,600	4,600	4,600
3,560	2,200	3,280	3,310	3,520	3,620	3,400
2,980	3,140	3,120	3,340	3,320	3,340	3,340
3,797	3,207	3,536	3,373	3,739	3,807	3,853
100%	84%	93%	94%	98%	100%	101%

TABLE 6.—*Rectal Operations*

On Admission	Days After Operation				
	1	2	3	4	5
4,290	4,080	4,590	4,530	4,550	4,590
3,170	3,500	4,170	4,200	4,210	4,350
3,680	3,600	3,680	3,670	3,690	3,680
4,210	4,120	4,250	4,100	4,100	4,170
4,460	4,680	5,000	4,800	4,900	4,950
4,300	4,820	4,820	4,500	4,440	4,440
4,480	4,100	4,560	4,510	4,560	4,560
3,820	3,120	3,450	3,420	3,450	3,450
4,116	3,940	4,252	4,216	4,238	4,274
100%	93%	103%	102%	103%	104%

days, the vital capacity continued steadily downward, the temperature rose slightly, and the patient showed clinical signs of bronchopneumonia. This diagnosis was confirmed by the roentgen-ray examination. Recovery was extremely slow. The temperature remained elevated until the twenty-seventh postoperative day and the vital capacity did not attain its preoperative level until the twenty-ninth day.

In spite of this stormy convalescence, the patient wished to have a left femoral hernia repaired before leaving the hospital. After the temperature had been normal for several days, this operation was performed under local and block anesthesia as before. The usual reduction in vital capacity occurred on the first postoperative day and a marked

and the temperature rose to 39 C. (102.1 F.). The physical examination was negative. The following day, the temperature was 40.6 C. (105 F.) and the vital capacity 820 cc. The physical examination and roentgenogram revealed pleurisy with effusion at the base of the right lung. Thoracentesis was performed twice during the next five days. Following this, the temperature fell by lysis, and the vital capacity gradually increased but did not attain its preoperative level. The patient was discharged on the forty-third postoperative day. On admission, the vital capacity was 4,450 cc.; on discharge 3,000 cc. (compare with chart 3).

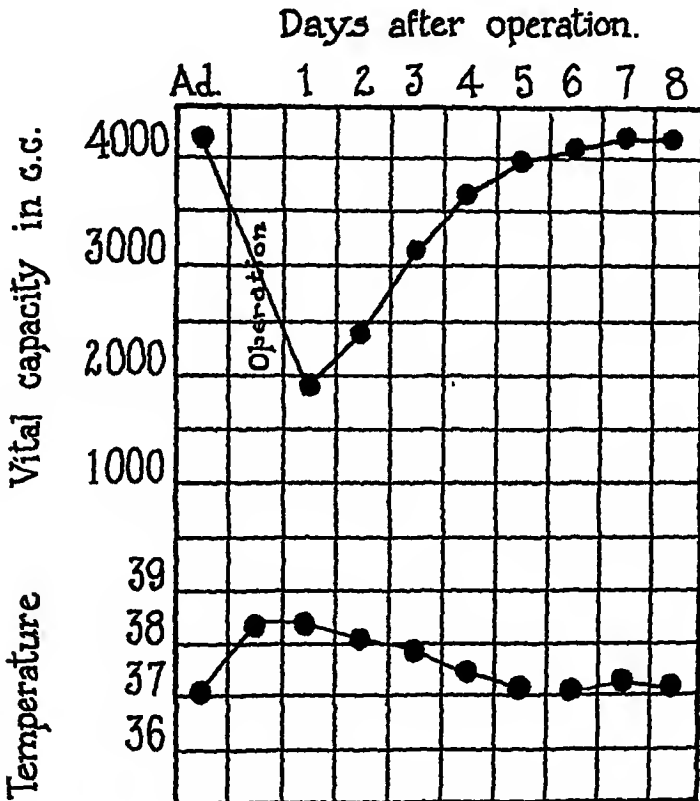


Chart 9.—Vital capacity of five patients on whom thyroidectomy was performed.

Chart 14 indicates the effect of postoperative abdominal complications on vital capacity. The patient was a well developed and well nourished man, aged 49. Following appendicectomy and drainage of an abscess under gas-oxygen-ether anesthesia, the vital capacity remained depressed and the temperature elevated. From this low level, a definite downward trend was noted on the sixth day, and rectal examination revealed a pelvic abscess. This was drained through the abdomen the following day. The vital capacity continued its downward course, and two days after the second operation, general peritonitis was present.

rise in temperature similar to that observed after the first operation. The temperature rapidly subsided, however, and the physical examination did not reveal evidence of any pulmonary complication. The vital capacity showed a normal upward trend and recovered its pre-operative level on the tenth day.

Chart 13 represents the vital capacity and temperature of a youth, aged 21, operated on for acute appendicitis. There was a marked fall in the vital capacity on the first postoperative day and a rapid recovery

TABLE 7.—Operations on the Extremities

On Admission	Days After Operation							
	1	2	3	4	5	6	7	8
4,400	4,460	4,400	4,400	4,500	4,480	4,480	4,480	4,480
3,220	3,150	3,240	3,320	3,370	3,320	3,360	3,410	3,380
4,100	4,350	4,340	4,350	4,350	4,350	4,350	4,350	4,350
3,290	2,050	2,140	1,900	2,300	2,000	2,400	2,750	2,830
4,800	4,780	4,860	4,860	4,860	4,860	4,860	4,860	4,860
3,490	3,450	3,460	3,400	3,510	3,450	3,510	3,510	3,510
4,210	4,320	4,290	4,280	4,320	4,320	4,320	4,320	4,320
3,220	2,420	2,510	2,650	3,150	3,200	3,160	3,290	3,260
4,000	3,650	3,750	3,810	3,850	3,700	3,790	3,810	3,850
4,500	4,510	4,720	4,710	4,710	4,710	4,710	4,710	4,710
3,580	3,800	3,520	3,600	3,700	3,700	3,800	3,880	3,790
4,050	3,630	3,180	3,620	3,800	3,840	3,930	3,900	4,000
4,900	4,600	4,650	4,880	4,900	4,900	4,900	4,900	4,900
2,610	2,540	2,520	2,390	2,600	2,600	2,450	2,550	2,670
4,710	4,430	4,420	4,690	4,750	4,700	5,000	5,000	5,000
3,937	3,716	3,747	3,804	3,911	3,931	3,935	3,951	3,995
100%	94%	95%	96%	99%	100%	100%	101%	101%

TABLE 8.—Thyroidectomy

On Admission	Days After Operation							
	1	2	3	4	5	6	7	8
4,790	2,100	3,400	3,880	4,140	4,300	4,520	4,890	4,900
3,200	1,360	1,680	2,350	2,800	2,900	3,120	3,220	3,220
4,500	1,800	2,090	3,100	3,560	4,150	4,500	4,500	4,500
4,400	910	1,750	2,840	3,600	4,420	4,400	4,400	4,400
4,350	3,450	3,100	3,640	4,110	4,220	4,360	4,390	4,350
4,248	1,924	2,400	3,155	3,642	3,928	4,180	4,280	4,274
100%	45%	57%	74%	85%	94%	98%	101%	101%

which on the eighth and ninth days had not reached the preoperative level. The temperature remained elevated and on the ninth day rose still higher to 39.5 C. (103 F.). On the tenth day, a marked reduction in vital capacity occurred but no clinical evidence of a pathologic process in the chest could be found. The temperature continued upward; on the eleventh day, there was a further reduction in vital capacity and physical examination revealed bronchopneumonia. In two days, the vital capacity fell from 3,920 cc. to 610 cc. During the next twelve days, the temperature gradually subsided to normal and the vital capacity increased to 2,690 cc. On the twenty-third day, the patient complained of thoracic pain on deep inspiration; the vital capacity fell to 1,290 cc.



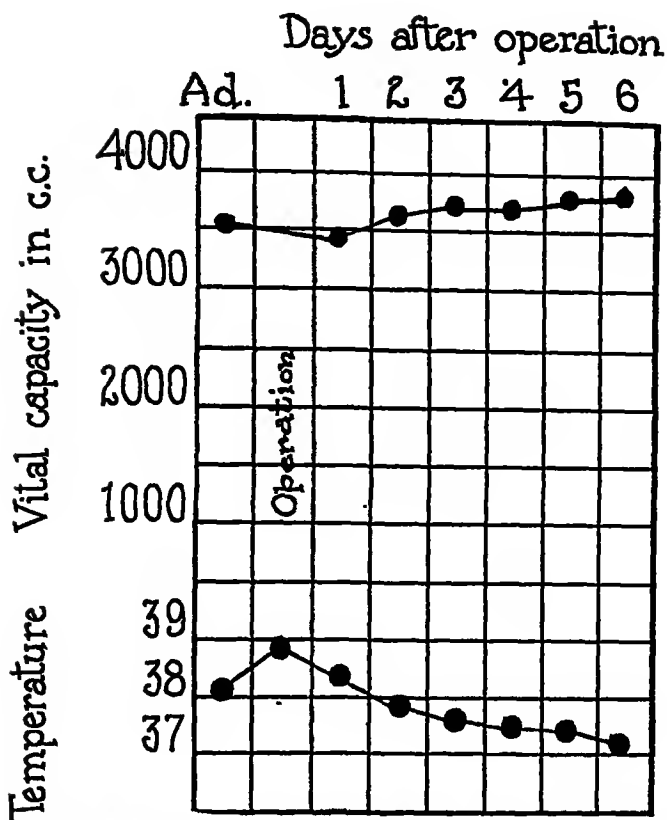


Chart 10.—Vital capacity of four patients subjected to other operations on the neck.

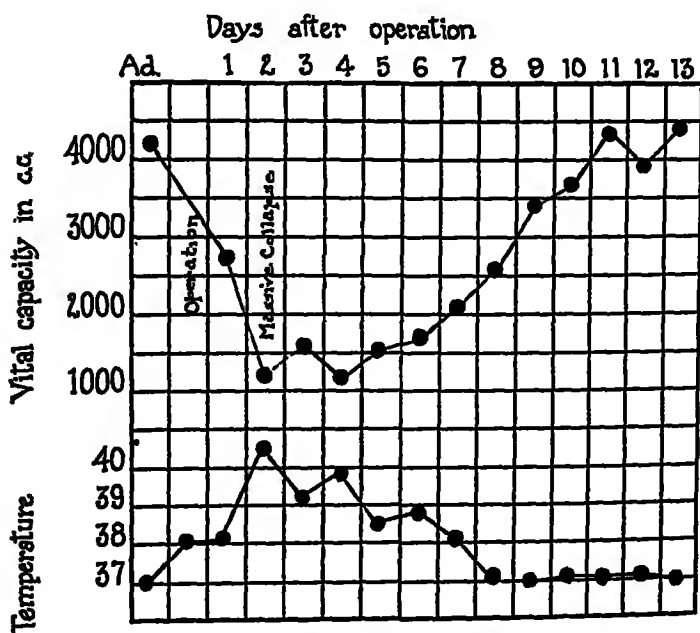


Chart 11.—Vital capacity and temperature of a patient on whom operation for unilateral hernia was followed by massive collapse of the right lung.

During the next five days, the vital capacity remained at essentially the same level and the temperature at 38 C. (100.4 F.). The patient was extremely sick; his pulse was weak and rapid; the abdomen was spastic and distended. On the sixth day after the development of general peritonitis, a definite improvement occurred in his clinical condition; the vital capacity was higher and the temperature lower. From then onward there was a gradual but steady upward trend to the vital capacity curve. The temperature returned to normal almost immediately (compare with chart 3).

Chart 15 illustrates the effect on the vital capacity of appendectomy complicated by general peritonitis. The patient was a well developed and well nourished colored man, aged 26. The preoperative vital capacity was somewhat below normal. Because of this, the subsequent decrease on the first postoperative day was less than usual. On the second day, the patient showed clinical evidence of generalized peritonitis and a further reduction in vital capacity occurred. During the next

TABLE 9.—*Other Operations on the Neck*

On Admission	Days After Operation					
	1	2	3	4	5	6
3,610	3,400	3,550	3,820	3,900	4,000	4,020
3,620	3,440	3,510	3,690	3,720	3,720	3,720
3,880	3,300	3,420	3,700	3,610	3,700	3,700
3,720	3,620	3,750	3,670	3,620	3,600	3,810
3,582	3,440	3,632	3,720	3,720	3,805	3,820
100%	90%	101%	104%	104%	100%	100%

three days, his vital capacity and clinical condition remained essentially the same. On the sixth postoperative day, a slight improvement was noted in both. Recovery was slow. He was discharged on the twenty-first day; the vital capacity was 3,200 cc. on discharge, 1,850 cc. on admission (compare with chart 3 and 14).

Chart 16 represents the vital capacity and temperature of a white man, aged 34, subjected to cystectomy and transplantation of the ureters into the rectum because of carcinoma of the bladder. The usual reduction in vital capacity occurred on the first postoperative day, accompanied by a rather marked elevation of temperature. On the third day, the vital capacity had increased slightly and the temperature had subsided to 38.2 C. (100.7 F.). On the fourth day, however, a secondary reduction in vital capacity was apparent and the temperature had again risen to 38.8 C. (101.4 F.). Examination of the patient revealed evidence of general peritonitis. The following day, there was a slight improvement in the vital capacity. This was only temporary, however, and the general trend was downward until death occurred on the thirteenth day after operation (compare with chart 5).

thyroidectomy is hard to explain. Possibly exposure of the trachea, retention of mucus, congestion and edema of the air passages may have some bearing on it. It may be that the excitement, apprehension and psychic instability characteristic of the majority of patients after thyroidectomy secondarily restrict their voluntary respiratory control.

By far the greatest reduction occurs when the operative incision is located in the upper part of the abdomen and invades the epigastric triangle. There is still a veil of mystery obscuring the accuracy of knowledge regarding the effect of upper abdominal operations. Cutler

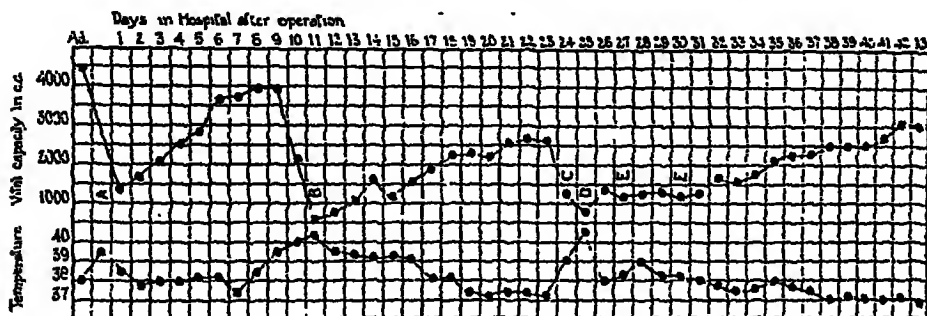


Chart 13.—Vital capacity and temperature curves of a patient on whom appendicectomy was performed; bronchopneumonia and pleurisy with effusion followed. *A* indicates operation; *B*, bronchopneumonia; *C*, pain on effusion; *D*, pleurisy with effusion; *E*, thoracentesis.

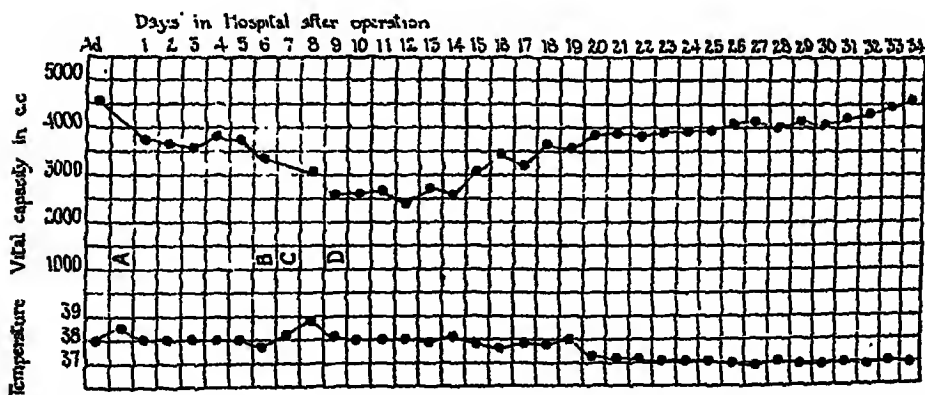


Chart 14.—Vital capacity and temperature curves of a patient on whom appendicectomy was performed; a residual pelvic abscess was drained and general peritonitis developed. *A* indicated operation; *B*, pelvic abscess; *C*, drainage and *D*, general peritonitis.

and Hunt<sup>17</sup> found that postoperative pulmonary complications occur in 8 per cent of epigastric operations, 4 per cent of laparotomies and 2 per cent of all operations. They attributed this to greater mobility of the field during operation and the consequent greater freedom with which multiple small emboli may be dislodged. Subsequent to epigastric

17. Cutler and Hunt (footnote 9 and 10).

No other postoperative complications developed, and consequently no curves are available for comparison with normal curves following operations on the upper part of the abdomen, extremities, neck or rectum.

## COMMENT

Since this work was started, two articles have appeared on vital capacity before and after operation. The curves presented in this paper compare favorably with those of Churchill and McNeil<sup>15</sup> and Head.<sup>16</sup>

It is evident from an analysis of the charts and tables that abdominal operations produce a tremendous immediate decrease in vital capacity followed by a gradual return to normal. There is an apparent similarity in the curves for each type of operative incision.

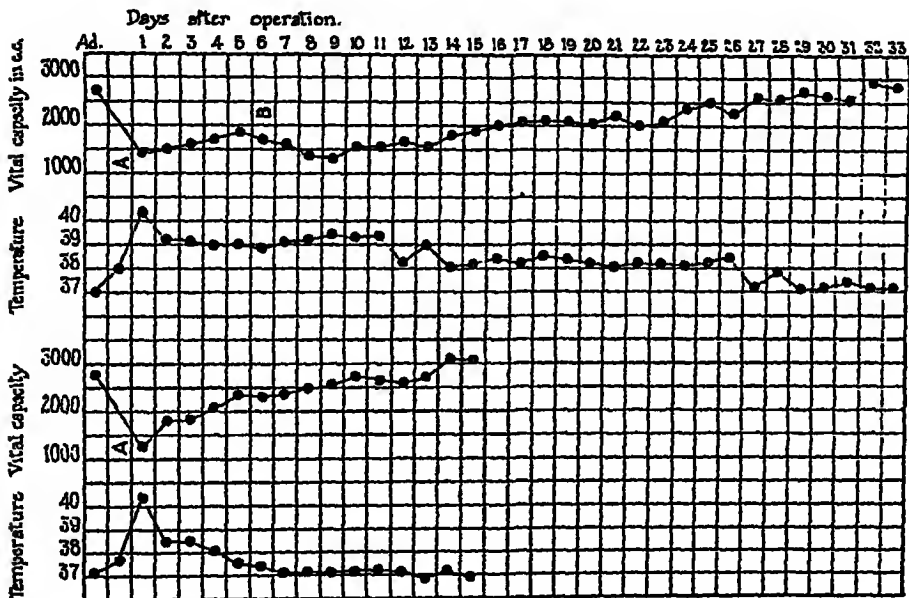


Chart 12.—Vital capacity and temperature curves of a patient operated on for right inguinal hernia; postoperative bronchopneumonia followed; an operation for left femoral hernia was attended by a normal convalescence. *A* indicated operation; *B*, pneumonia.

Partial removal of the thyroid gland likewise entails an immediate and pronounced fall in the vital capacity followed by a rapid recovery. All other operations on the neck and those on the extremities and rectum have no effect on the vital capacity. The reason is obvious; the muscles of respiration are not involved in the operative incision. Why the vital capacity should be so profoundly, though temporarily, affected by

15. Churchill, E. D., and McNeil, D.: The Reduction in Vital Capacity Following Operation, *Surg. Gynec. Obst.* 44:483, 1927.

16. Head, J. R.: The Effect of Operation Upon the Vital Capacity, *Boston M. & S. J.* 197:83, 1927.

# ASCARIASIS OF THE GALLBLADDER

## LITERATURE AND CASE REPORT

CHARLES BRUCE MORTON, M.D.

Assistant Professor of Surgery and Gynecology, in the University of Virginia  
UNIVERSITY, VA.

Ascariasis is not usually grouped among the diseases requiring surgical intervention, and its presence in what may be called a surgical form is probably seldom diagnosed prior to operation. Ascariasis of the gallbladder is especially unusual, if one may judge by the infrequency with which it has been recorded in the literature. The finding of an ascarid in the gallbladder of a woman on whom I recently performed an operation for cholecystitis suggested this study.

### LITERATURE

The literature contains numerous references to cases in which ascarids were found in other unusual sites: the urinary passages, the appendix, the pancreatic duct, the common bile duct and the hepatic ducts. Ascarids in these locations were credited with causing many types of symptoms, chiefly those of obstruction and inflammation, presenting, however, few if any pathognomonic peculiarities. DaCosta<sup>1</sup> in his textbook on surgery, does not mention ascariasis among the diseases of the gallbladder. Only three direct references to the presence of parasitic worms in the gallbladder were found in the literature. Of the many other articles indexed under "ascariasis," "gallbladder," and other heads, only the more likely were investigated. In this group, only five additional articles were found in which ascariasis of the gallbladder was mentioned.

In 1765, Lorry,<sup>2</sup> quoted by Aviles, recorded the first case found in the literature. He cited the case of an insane patient in whose gallbladder three ascarids were found at necropsy. This patient vomited a worm prior to death and died in convulsions, presumably caused by the presence of the parasites in the gallbladder. Aviles<sup>3</sup> recorded a case of ascariasis of the gallbladder encountered at operation and summarized

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1. DaCosta, J. C.: *Modern Surgery*, ed. 9, Philadelphia, W. B. Saunders Company, 1925.

2. Lorry, A. C.: *De melancholia et morbis melancholicis* 16:339; 8:429, Lutetiae Parisiorum. P. G. Cavelier, 1765.

3. Aviles, J.: *The Rôle of Ascariasis in Gallbladder Disease*, Surg. Gynec. Obst. 27:459, 1918.

operations, there is a more complete and prolonged splinting of the abdomen and lower part of the thorax, with the result that the respiratory movements are more grossly impaired over a longer period of time than after operations on any other part of the body. May not this pulmonary embarrassment and comparative immobility play some part in the more frequent occurrence of postoperative complications follow-

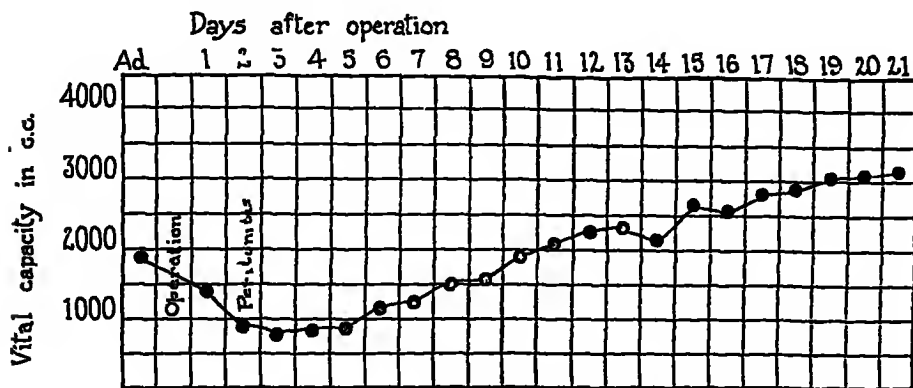


Chart 15.—Vital capacity of a patient subjected to appendicectomy for ruptured appendicitis and general peritonitis.

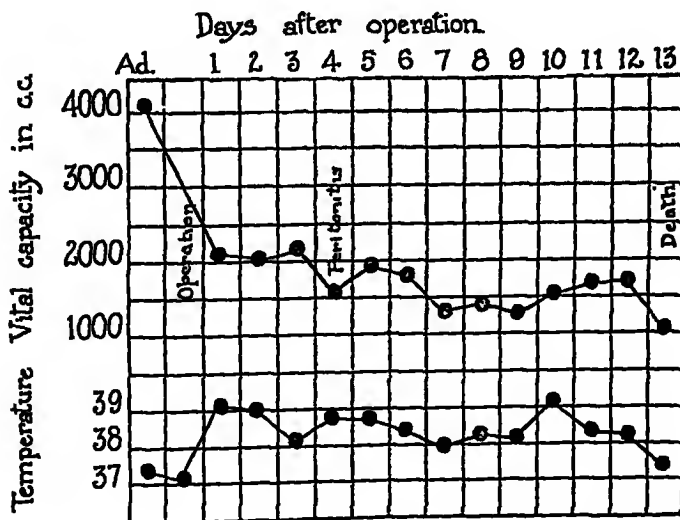


Chart 16.—Vital capacity of a patient subjected to cystectomy and transplantation of the ureters; general peritonitis developed and death ensued.

ing upper abdominal incisions? Karsner and Ash<sup>18</sup> showed experimentally that a partially atelectatic lung offers a more fertile soil for the reception of emboli than one which is normally aerated. The sequence of events seems logical. Most upper abdominal incisions are placed to the right of the midline; consequently, expansion of the lower lobe of

18. Karsner, H. T., and Ash, J. E.: Studies in Infarction: II. Experimental Bland Infarction of the Lung. *J. M. Research* 22:205, 1912-1913.

worms as short as  $1\frac{1}{4}$  inches (3.1 cm.) in length in the bile ducts. Stiles<sup>11</sup> said: "The eggs of the ascaris will not hatch as long as they are in the human body. They must pass out and there undergo their changes. The young worm is developed inside the egg, the egg is then swallowed, hatches out in the stomach, crawls through the wall of the stomach, gets into the circulation, goes to the heart and lungs, up the trachea, down through the stomach to the small intestine, and there develops further." Others differ with this opinion and believe that ova which contain embryos and which are still surrounded with the mulberry envelop will develop into roundworms in the human intestine.

The cases of ascariasis of the gallbladder were not recorded in anything approaching a uniform manner. There are, however, certain similarities in all of them which form a rather clearcut composite picture.

The data in the two cases quoted by Devaine were very meager and the brief facts of Lorry's case have already been quoted. The cases of ascariasis reported by Aviles, Tyau, Eberle, and Butt and the case of taeniasis reported by Benedict were complete enough for instructive study, and I shall summarize them.

#### REPORT OF CASES

**AVILES' CASE.**—A woman, aged 38, had suffered with attacks of pain in the upper part of the right side of the abdomen for twenty-six years. Attacks had been increasingly severe for the last year. She had occasionally vomited roundworms. For six days before admission to the hospital she suffered continuous pain, which radiated to the right shoulder blade and was accompanied by slight icterus and moderate fever. The diagnosis of cholecystitis with probable cholelithiasis was made, and the abdomen was explored. An *Ascaris lumbricoides* 8 inches (20.32 cm.) in length was found in the gallbladder obstructing the cystic duct. The worm was removed, and a cholecystostomy was performed. Anthelmintics were administered during the postoperative convalescence.

**TYAUS' CASE.**—A man, age not mentioned, had suffered for three months with epigastric pain which radiated to the liver region but not to the shoulder. A mass suspected of being the gallbladder was palpable. Ova of *Ascaris lumbricoides* and *Trichuris trichiura* were found in the stools. Santonin was administered and eighteen roundworms evacuated, but the symptoms were not relieved. Five days later, the patient died. Necropsy disclosed nine roundworms occluding the cystic duct. There were multiple abscesses of the liver and several roundworms in the hepatic ducts. Ova were found in the gallbladder, the biliary ducts and the liver itself.

**EBERLES' CASE.**—A boy, aged 9 years, had been treated with santonin for intestinal parasites. Five months later, he complained of pain in the upper part of the right side of the abdomen, and there were symptoms of jaundice. The abdomen was explored for gallbladder disease, and a living roundworm was found in the gallbladder. Three more worms, all alive, were found in the hepatic duct.

**BUTT'S CASE.**—A woman, aged 30, mother of three children, had had six attacks of severe pain in the upper part of the right side of the abdomen during

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11. Stiles, C. W.: Personal communication to Butts.

the literature. He quoted two other authors, Bonfils<sup>4</sup> (1858) and Devaine<sup>5</sup> (1860), who had recorded "a few cases." Bonfils quoted Lorry, Devaine quoted Lorry's case and two other cases which were attributed to Heaviside and Bloch.

In 1922, Butt<sup>6</sup> added a case of his own to the literature and quoted Tyau<sup>7</sup> (1920) and Eberle<sup>8</sup> (1920), who reported two more cases. Up to the time of this writing no other cases of ascariasis of the gallbladder were found in the literature. However, Benedict,<sup>9</sup> in 1926, reported a case in which *Taenia saginata* was found in the gallbladder. Because of its similarity to the cases in which *Ascaris lumbricoides* was present in the gallbladder, it is probably of more than passing interest.

That animals as well as man may harbor ascarids in the gallbladder was ascertained from Schlotthauer.<sup>10</sup> He, dealing with numerous laboratory and domestic animals, stated that he had occasionally encountered ascarids in the gallbladder of swine. They were apparently an incidental observation, and no symptoms or pathologic changes were ascribed to their presence.

Aviles called attention to the wide and almost universal geographic distribution of *Ascaris lumbricoides*, and said that the pathogenicity of the parasite depended on three characteristics. The first was a poisonous material found in extracts of the worm; the second was the carrying of infection by the motile and migratory traits of the ascarid, and the third was mechanical, the obstruction in a hollow viscus sometimes caused by a parasite or group of parasites. The last two characteristics are of primary importance in considering ascariasis of the gallbladder.

Another important consideration is the life cycle of the parasite. Knowledge of this is necessary in attempting to determine whether an ascarid found in the gallbladder has come there as an ovum and subsequently hatched, or whether its presence there is the result of migration of a worm from the intestine. Ova of *Ascaris lumbricoides* were found in the gallbladder and bile ducts by Tyau, and he also found

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4. Bonfils, E. A.: Des lésions et des phénomènes pathologiques déterminés par la présence des vers ascarides lombricoïdes dans les canaux biliaires, p. 28, Paris, Rignoux, 1858; reprinted from Arch. gén. de med., Paris, 1858.

5. Devaine, C.: Traité des entozoaires et des maladies vermineuses de l'homme et des animaux domestiques, Paris, 1860, p. 156.

6. Butt, A. P.: Round Worm (*Ascaris lumbricoides*) in Gallbladder, Surg. Gynec. Obst. 35:215, 1922.

7. Tyau, E. S.: Pathogenicity of *Ascaris lumbricoides*; Report of Cases, M. J. China, 6:21, 1920; abstr., J. A. M. A. 75:135 (July 3) 1920.

8. Eberle, D.: Ascarids in the Liver and Pancreas, Schweiz. med. Wchschr. 50:1110, 1920; abstr., J. A. M. A. 76:344 (Jan. 22) 1921.

9. Benedict, E. B.: *Taenia Saginata* in the Gallbladder, J. A. M. A. 87:1917 (Dec. 4) 1926.

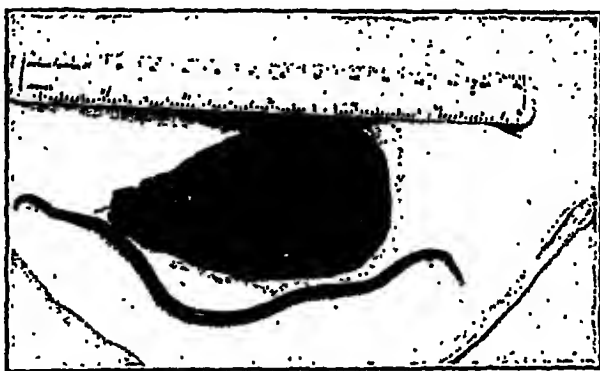
10. Schlotthauer, C. S.: Personal communication to the author.



following intravenous injections of dye (tetra-iodo-phenolphthalein) failed to show any trace of a shadow of the gallbladder. Subacute cholecystitis with probable cholelithiasis was the diagnosis made, and an operation was advised.

On Nov. 17, 1927, I made a high incision through the right rectus muscle and explored the abdomen. The pelvic organs, appendix, kidneys, stomach and duodenum apparently were normal. The gallbladder was surrounded with recent adhesions to adjacent structures and was distended to a diameter of about 8 cm. at the fundus. Stones were not palpated, and the gallbladder did not empty under pressure. The walls were thickened. The common bile duct was not enlarged, and stones were not palpated in it. The gallbladder was removed from below outward, and the abdomen closed without drainage.

Pathologic examination of the gallbladder disclosed thickening and subacute inflammation of the walls. The mucosa showed some cholesterol deposits. The bile was of about normal consistency. In the gallbladder was discovered a living, actively motile roundworm, *Ascaris lumbricoides*, which measured 17.5 cm. in length (fig. 1).



Ascarid and gallbladder removed from patient.

Postoperative convalescence was quite uneventful, and the patient was allowed to go home on Dec. 4, 1927, eighteen days after her operation. Anthelmintics were advised to rid her of any parasites remaining in the intestinal tract.

Following the unusual and unexpected operative observation, the patient was carefully questioned concerning her previous history. She again denied any former attacks of pain in the gallbladder region, and said that she did not know that she harbored intestinal parasites until the day before operation. On that day she was nauseated and vomited an *Ascaris lumbricoides* 15 cm. in length.

#### COMMENT

The problem of how a parasitic worm may have arrived in the gallbladder is one difficult to solve. One must assume either the hatching of an ovum in the gallbladder or the migration from the intestine of a worm sufficiently small to pass through the cystic duct. In Benedict's case, a taenia 10 feet (304.8 cm.) long was found in the gallbladder. How long this parasite had been in the gallbladder is not easy to determine, although it is improbable if not entirely impossible to suppose that it could have passed through the cystic duct while measuring anything approximating 10 feet in length.

two years. She had frequently passed roundworms in her stools. When seen she had suffered pain for six days, and a diagnosis of cholecystitis with probable cholelithiasis was made. Operation disclosed a distended but otherwise rather normal looking gallbladder. It was incised, and a roundworm about 5 inches (12.74 cm.) in length was removed. No stones were found. The incision in the gallbladder was closed, and the abdomen was closed without drainage.

In the next case, *Toxocara saginata* was found in the gallbladder. This case is summarized because of its similarity to the cases of ascariasis of the gallbladder and because of the great length attained by the worm.

**BRUNTON'S CASE.**—A man aged 74, had had several previous attacks of pain in the upper part of the right side of the abdomen which were not accompanied by jaundice. The patient had known for two years that he harbored a tapeworm, and he remembered eating morsels of raw beef when he was a boy, many years before. Ten days after an operation for cataract, he was seized with severe pain in the upper part of the abdomen, and a diagnosis of acute cholecystitis was made. The abdomen was opened, and three gallstones and *Toxocara saginata* of 15 and 2 inches (38.1 cm., in length) were found in the gallbladder. Cholecystectomy was performed.

After, from his study of the subject, concluded that such cases are rare, and that the diagnosis is not easy. He pointed out that the finding of an ascariis complicating an attack of gallbladder pain is not made one suspects the possibility of ascariasis of the gallbladder and is an indication for exploration of the abdomen. Furthermore, it strongly advised the use of anthelmintics as a prophylactic and therapeutic measure. He concluded that cholecystectomy is probably the treatment of choice in view of the fact that the eggs remain in the gallbladder and lead to a recurrence of the disease.

**HOWARD'S CASE.**—A 37-year-old male, the wife of a Virginia farmer, married the University of Virginia Hospital on Nov. 12, 1935. Her family history was unimportant and her past illness was apparently negative. She had had the following symptoms: pain in the upper right abdomen, which was intermittent and was relieved by the use of the stomach pump. The pain had been present for some time and the onset of the present attack was

On admission the patient was that she had suffered the pain in the upper part of the abdomen for five years. The pain was described by her as "colic" which occurred while she was eating. She stated that the first attack occurred in a few moments and was followed by a severe pain in the upper part of the right side of the abdomen. The pain was described as "sharp" and "stabbing" and was relieved by the use of the stomach pump. After a few hours the pain gradually subsided and she was able to eat and sleep. The patient was examined on the day of admission and was found to be in good health. The abdomen was examined and was found to be normal. The patient was discharged on the day of admission and was found to be in good health.

Examination of the patient disclosed a diagnosis of ascariasis of the gallbladder. The patient was treated with anthelmintics and was found to be in good health. The patient was discharged on the day of admission and was found to be in good health. The patient was discharged on the day of admission and was found to be in good health.

I made a tabulation of the cases of ascariasis found in the literature and included my own case and that of Benedict, in which the parasite was not an ascarid but *Taenia saginata*. The incidence in the two sexes is about equal, and the age limits vary between 9 and 74 years. There are two factors, however, which are constant in every case; the history of intestinal infestation with parasites and symptoms referable to the gallbladder.

These two constant features of the cases do not assure the diagnosis, but when elicited they should at least lead one to bear in mind the possibility of ascariasis of the gallbladder.

The treatment for ascariasis of the gallbladder is the same as that for inflammation or obstruction of the organ due to other causes. As suggested by Butt, cholecystectomy is probably the operation of choice. Anthelmintics are indicated as a prophylactic measure in all persons with intestinal parasites and as a postoperative measure in ascariasis of the gallbladder to rid the patient of any remaining parasites.

#### SUMMARY

The literature was searched for cases of ascariasis of the gallbladder. Seven cases were found and five have been briefly summarized. A case of taeniasis of the gallbladder was found and also summarized. It was similar in many respects to the cases of ascariasis. All cases had been diagnosed only after operation or necropsy.

A case of ascariasis of the gallbladder which I encountered has been described, and the condition discussed in relation to its etiology, diagnosis and treatment. It was pointed out that the disease is rare and difficult to diagnose. Furthermore, the treatment is surgical and cholecystectomy is probably the operation of choice. Anthelmintics are indicated for prophylactic use and postoperatively. The history of ascariasis in a patient with signs of cholecystic disease should always suggest the possibility of ascariasis of the gallbladder.

Probably the preoperative diagnosis of ascariasis of the gallbladder will never be made with any great degree of certainty. In the first place, it is obviously a rather rare condition and one which would hardly be thought of unless one were to bear it in mind in all cases of cholecystic disease. In the second place, the symptoms of the disease do not differ in general from those of the commoner varieties of inflammation and obstruction of the gallbladder and cystic duct.

*Outline of Cases Found in Literature and of My Own Case*

Case Reported by	Sex	Age	Past History		Complaint	Pre-operative Diagnosis	Observations at Operation	Results
			Ascariasis	Gallbladder				
Heavyside and Bloch, quoted by Devaine, 1800	2 cases, were not recorded in detail							
Lorry, 1765...	..	..	Vomited an ascarid	.....	Convulsions	.....	.....	Necropsy: three ascarids in gallbladder
Aviles, 1918...	F	38	Vomited ascarids occasionally	Periodic attacks for 26 years	Gallbladder colic for 6 days	Cholecystitis; probable cholelithiasis	Ascarid 8 inches long in gallbladder	Cholecystostomy
Tyan, 1920....	M	..	Ova found in stools	Pains for 3 months	Pain and mass in gallbladder area	.....	.....	Necropsy: nine ascarids in cystic duct
Eberle, 1920...	M	9	Treated for ascariasis 5 months previously	Pain and jaundice	Pain and jaundice	Cholecystitis	Ascarid in gallbladder	Cholecystostomy presumably
Butt, 1922....	F	30	Frequently passed ascarids in stools	Periodic pain for 2 years	Gallbladder colic for 6 days	Cholecystitis; probable cholelithiasis	Ascarid 6 inches long in gallbladder	Gallbladder closed without drainage
Benedict, 1926	M	74	Known to have taenia 2 years; raw beef eaten 50 years before	Several attacks previously	Gallbladder colic for few hours	Acute cholecystitis	Taenia 10 ft. 2 in. long found in gallbladder	Cholecystostomy
Morton, 1928..	F	45	None except vomited ascarid day before operation	None	Gallbladder pains for 5 weeks	Cholecystitis; probable cholelithiasis	Ascarid 17.5 cm. long found in gallbladder	Cholecystectomy

The case reported herewith illustrates the point. The history and physical observations were similar to those in numberless other cases of ordinary cholecystic disease. The laboratory and cholecystographic data were equally commonplace. The diagnosis of cholecystitis with probable cholelithiasis seemed obvious.

There was, however, one fact not taken into consideration in making the diagnosis. That was the vomiting of the ascarid the day before operation, ignored as not important at the time and yet in the light of subsequent observations it proved to be one of the most significant features of the case.

The ureters are located and severed between small artery forceps as near to the bladder as possible. The distal stump is cauterized with phenol and ligated. The proximal end of the ureter is liberated for 7.5 or 10 cm. by slitting the peritoneum over it. Ureteral catheters, provided with rubber cuffs to prevent slipping, are inserted into the ureter. A strong linen thread is passed twice around the ureter and cuff and tied tightly with a double or surgeon's knot. A similar suture is then tied around the ureter below the incision to prevent infection ascending the ureter from the bowel. Urine usually begins to escape from the catheters at once.

To avoid too much narrowing, one incision should be higher in the bowel than the other. The incision should begin near the mesenteric edge and extend downward and obliquely toward the antemesenteric border to avoid as many of the large vessels as possible. It should be about 3.8 cm. in length, and through the peritoneum and muscle, thus permitting the mucosa to pouch out partially. A small stab wound is made in the mucosa between traction sutures. A little of the gauze already inserted in the rectum is picked up with mosquito forceps, and to this the end of the cathéter is attached. After both of the catheters are attached to the gauze, the gauze is gradually withdrawn from the rectum and in so doing the ureteral ends are drawn into the openings in the mucosa. The catheters must be marked to indicate the right and left kidney. After the ureter is drawn past the ligature, the free ends of the two traction loops are tied across the ureter to close the opening partially. These traction loops, inserted before the mucosal puncture, are important in handling the intestine.

[ED. NOTE.—Coffey's method of ureteral transplantation is, at the present time, accepted by most urologists as the one giving the most satisfactory functional results. Not all urologists agree as to the indications for ureteral transplantation. Hinman<sup>27</sup> believes in transplanting the ureters into the bowel in a small group of cases. Usually this method is employed now only as a last resort, but if freed from some of its dangers, it could be applied to a larger number of cases. Hinman believes that a surgical victory over this defect must include restoration of natural relationships. To insure satisfactory renal function, a first stage preparatory nephrostomy should be performed; this is followed subsequently by ureteral transplantation.]

Marion<sup>28</sup> states that ureteral transplantation is of doubtful value. If it is performed, it is necessary to be ready to operate on the corresponding kidney in case of complications. In some cases, instead of

27. Hinman, Frank: 'The Indication of Nephrostomy Preliminary to Uretero-rectoneostomy, J. A. M. A. 86:921 (March 27) 1926.

28. Marion, M.: Suite de la discussion sur les implantations urétérales, J. d'urol. méd. et chir. 20:58, 1925.

# A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.  
LOS ANGELES

E. STARR JUDD, M.D.  
ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.  
ROANOKE, VA.

GORDON S. FOULDS, M.D.  
TORONTO

JEAN VERBRUGGE, M.D.  
ANTWERP, BELGIUM

AND  
ADOLPH A. KUTZMANN, M.D.  
LOS ANGELES

*(Continued from page 178)*

## URETER

*Transplantation.*—Peterson<sup>25</sup> believes that the extraperitoneal route is more desirable than the intra-abdominal in the transplantation of the ureters into the bowel. Even with the most skilful care, the wound may become infected, and tight approximation of the suture line is difficult. If urine or feces escape around the opening through the mucosa, the patient usually succumbs, unless the operation has been performed extraperitoneally. Technically, it is not more difficult since the ureters are readily exposed and easily transplanted.

Peterson reports several cases of incurable vesicovaginal fistula in which transplantation of the ureters was carried out in order to secure sphincteric urinary control. He does not expose the patient to the additional risk of transplanting both ureters at the same operation.

In Coffey's<sup>26</sup> earlier papers, he advises the insertion of a small rubber tube into the ureter before transplantation. The greatest trouble in ureteral transplants, especially in animal experimentation, is infection emanating from the opening in the intestine. At present, Coffey uses the following technic: The bowel is cleansed with castor oil and enemas before operation. The abdomen is opened low near the median line, and the sigmoid is pulled down into the field of operation. A sigmoidoscope is inserted into the rectum, and the lower part of the bowel is flushed by a pointed cannula inserted through the wall of the sigmoid. The rectum is then packed full of dry gauze, and the sigmoidoscope is removed.

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25. Peterson, Reuben: Transplantation of the Ureters into Bowel to Secure Sphincteric Urinary Control in Incurable Vesicovaginal Fistula, *Am. J. Obst. & Gynec.* 14:492, 1927.

26. Coffey, R. C.: Completed Aseptic Technique for Implantation of Ureter into Large Bowel, *Surg. Gynec. & Obst.* 45:816, 1927.

in man. The fundamental requisite is a sustained tonic contraction of the musculature of the bladder as it actively resists distention. Atonic bladders never regurgitate; postmortem experiments are futile. Moreover, as Graves has shown, there are no intrinsic anatomic differences, such as have been claimed, between the ureterovesical relationship of the laboratory animal and of the human being.

In general, then, it may be stated that there are two groups of bladders so far as reaction to distention is concerned. One group, marked by an active state of muscle tone, resists distention, and in these tracings of intravesical pressure show a constant, relatively rapid, rise of tension as filling proceeds. Such bladders will regurgitate when the normal outlet is obstructed in a large percentage of cases, as he has demonstrated in a long series of observations on animals. The other group, in which tone is relatively lacking, consists of bladders that offer feeble or no resistance to the force of distention. These bladders fall away from the distending fluid, and there is no appreciable sustained rise in intravesical pressure until the end-stage of filling is reached, when, as has been said, a purely mechanical tension is produced because the sac can hold no more. In this passive type of bladder, regurgitation does not occur.

As Graves was dealing with fundamental reactions of smooth muscle, it seemed reasonable to expect in starting this particular investigation that the bladder of man, in its behavior during distention, would fall into one or the other of these groups and so give further evidence of support or denial of the clinical theory of regurgitation. To answer this phase of the question, he has made use of an instrument which has just been completed and which makes it possible to record accurately the development of intravesical pressure during filling of the bladder. The instrument consists of a reservoir from which the bladder may be filled with a definite volume and rate of speed through the action of a small piston pump. There is also a mercury manometer which communicates with the recording device and which is in open communication with the cavity of the bladder throughout the period of filling. Geared to the pump is a small kymograph which provides the permanent record of the manometer as it registers the changes in intravesical tension.

Thus far, however, he has noted only one case, that of a long-standing stricture with infection, which would not be classified beyond question with the active tonic group of bladders that he has described experimentally and that permitted reflux in so large a percentage of cases. Only the atonic bladder of disease of the spinal cord was of the passive type. The curves for the human being are similar to those for animals; from this analogy, Garves claims support for the probability of regurgitation in the bladder of man.

reimplantation, primary or secondary nephrectomy may be desirable. He believes that in most cases the kidney of the ureter that has been transplanted becomes dilated and gradually atrophies. Legueu, in discussing Marion's statements, states that he has noted only one favorable case of transplantation reported in the literature, that of a patient who, seventeen years after transplantation of the ureter, still had a well functioning kidney.

Papin<sup>29</sup> states that in his experience, ureteral transplantation is more satisfactory than simple nephrostomy. Isolation of the ureter from its normal connections disturbs its functioning power: it becomes atonic and dilated and contracts more slowly and less frequently. All surgical procedures on the ureter cause infection; the resulting dilatation of the ureter is responsible for most ascending infections. Papin gives three methods of transplanting the ureter: transplantation to the skin, transplantation into the urethra and transplantation into the intestine. He believes that the transplantation to the skin is the safest of the three methods.

Smitten<sup>30</sup> compiled a series of 318 cases of implantation of the ureters into the intestine with the following results: fistula of the bladder, 156 cases, with death in 34 (21.8 per cent); anomalous conditions, 58 cases, with death in 18 (31 per cent); malignant tumors, 98 cases, with death in 61 (63 per cent), and inflammatory processes, 4 cases, with death in 3 (75 per cent). Of the total number of patients, 116 died and 200 recovered; in 2 cases the result was not known. Thirty patients died from peritonitis, 21 from urinary infection, 5 from pneumonia and 3 from tuberculosis. The late results, from six months to ten years, were known in 71 cases. In 6 of these death was caused by renal insufficiency, in 3 by recurrence of the original condition, and in 2, by intercurrent disease.

In many cases, the time consumed and the difficulty of the operation do not justify the attempt to preserve renal tissue. The ureter is often already dilated and infected and the corresponding kidney is only slightly infected. On the other hand, in certain cases, such as exstrophy of the bladder in young patients, ureteral transplantation is unquestionably a life-saving procedure.

*Regurgitation.*—Graves,<sup>31</sup> in continuing his studies on regurgitation from the bladder into the ureters under normal conditions at the ureterovesical juncture, investigated the pressure curve of the bladder

29. Papin, M.: La dérivation haute des urines, *Presse méd.* 2:1412, 1925.

30. Smitten, A. T.: Ueber die Einpflanzung der Ureteren in den Darm, *abstr. Ztschr. f. urol. Chir.* 19:219, 1926.

31. Graves, R. C.: IV. Studies on the Ureter and Bladder with Especial Reference to Regurgitation of Vesical Contents; Bladder Pressure-Curve in Human, *J. Urol.* 18:321, 1927.



is always dangerous and should be performed only when other tests of renal function give good results.

Suitable preoperative treatment usually results in reestablishing renal function and in rendering the patient fit for prostatectomy. In some cases, the function of the kidney cannot be improved sufficiently by catheter drainage; in these, the two-stage operation should be performed.

Wildbolz believes that the perineal operation puts much less strain on the heart and lungs and causes less shock than the suprapubic. He finds that suprapubic prostatectomy is usually followed by an increase in the blood urea, lasting for several days, but after a perineal operation there is practically no such increase. The perineal operation does not cause nearly so much bleeding, and the perineal wound does not hinder respiration or expectoration. Furthermore, the perineal operation is not followed by necrosis of the tissues, and the wound is so well drained that there is only a slight amount of absorption which may increase the blood urea.

Wildbolz uses the same incision in performing perineal prostatectomy as that employed by Zuckerkandl, Albarran and Proust, with a slight modification used also by Young. The central tendon of the perineum is exposed and cleaned. A small transverse incision is made in it close to the bulb, and the recto-urethralis muscle is exposed. This is divided close to the urethra, and the prostate is exposed by blunt dissection. On the anterior wall of the wound are the bulb and transversus perinei muscle, and on the posterior side lies the rectum. The prostate is pressed down toward the perineum by a metal catheter introduced into the urethra. It is covered by the fascia of Dénonvillier. This fascia is divided transversely just above the apex of the gland and is pushed backward, exposing the posterior portion of the capsule in the wound. Wildbolz makes a vertical incision in the median line, commencing at least 1 cm. above the apex, which involves only the capsule of the prostate and does not penetrate to the urethra, and which enables one to distinguish between capsule and adenomatous masses. Both lobes of the prostate are enucleated as far as possible. The prostatic urethra is divided transversely just at the lower end of the adenomatous mass, the upper end still being left in connection with the neck of the bladder. Young's retractor is introduced through the prostatic urethra into the bladder, and the upper end of the urethra is divided close to the neck of the bladder, with any adhesions still existing between the adenoma and the capsule of the gland. The bladder is washed out to remove blood clots.

Four sutures are placed through the neck of the bladder, and afterward through the stump of the urethra at the apex of the gland. They unite the neck of the bladder to the urethra inside the prostatic cavity. Thus this procedure restores normal anatomic conditions as far as possi-

## PROSTATE

*Hypertrophy.*—Troell<sup>32</sup> reports his results in a series of 93 cases in which prostatectomy was performed, with 5.4 per cent primary mortality (82 cases of benign hypertrophy of the prostate with 4.9 per cent mortality and 11 cases of prostatic carcinoma with 9 per cent mortality). Troell accentuates the need for preoperative treatment, especially drainage of the bladder.

Four and three-tenths per cent of the patients had epididymitis; the occurrence of this condition can be limited by a frequent change of the urethral catheter both before and after operation. In the cases of carcinoma, permanent results following prostatectomy were not good; in some cases, recurrence and metastasis occurred six months after operation. Troell believes that metastasis to bone may be favorably influenced by repeated treatments with the roentgen rays.

Wildbolz<sup>33</sup> gives the following indications for prostatectomy: (1) permanent retention of a considerable quantity of urine in the bladder (from 150 to 200 cc. or more); (2) frequent attacks of complete retention; (3) long-standing infection of the bladder, and (4) severe repeated hemorrhage from the hypertrophied prostate.

He does not perform prostatectomy as a prophylactic measure. It is never a harmless procedure and is justified only when the patient is in real danger from disease. Wildbolz considers the water test one of the most important of all the tests for renal function. Suter of Basle refuses to perform an operation unless the urine concentrates to a specific gravity of at least 1.017. Lehmann considers 1.018 and Rubritius 1.015 to be the minimum. Wildbolz shows that these figures are unnecessarily high, as twenty-six of his patients recovered in spite of a much lower concentration of the urine. In eighteen, it was from 1.011 to 1.014; in seven, it was 1.010, and in one 1.009.

Negro and Colombet of Marion's Clinic state that operation should not be performed unless at least 42 per cent of phenolsulphonphthalein is eliminated in the first hour. Blanc considers 55 per cent as a minimum. The majority of Wildbolz's patients eliminated more than 30 per cent of phenolsulphonphthalein in the first hour, but thirteen eliminated from only 20 to 30 per cent and ten less than 20 per cent.

The observations of Wildbolz and other investigators show that prostatectomy will be followed by uremia if the urea of the blood is more than 100 mg. per hundred cubic centimeters, and probably so if it is over 80 mg. When the blood contains from 50 to 80 mg., the operation

32. Troell, Abraham: Prostatectomy: Some Remarks About Indications, Technique and Results, *Acta chir. Scandinav.* 62:133, 1927.

33. Wildbolz, Hans.: Indication and Execution of Prostatectomy, *Proc. Roy. Soc. Med., Sect. Urol.* 20:50, 1927.

these causes of death. Two types of cases present the greatest hazards in prostatectomy: those in which prolonged urinary retention has resulted in marked renal insufficiency, and acute uremia and death are readily precipitated by immediate prostatectomy; and those in which the urinary tract is free from infection, only a few ounces of urine are retained as the result of prostatic obstruction, and there is little or no impairment of renal function, a type of case in which general sepsis is likely to be precipitated by immediate prostatectomy. Experience has taught that in the first type the patient may recover from actual or potential uremia, that renal efficiency may be restored or approach normal, and that the cardiovascular renal reserve may be increased by a period of careful and adequate preoperative treatment. In the second type of case, the patient may likewise be provided with immunity to infection by the same means.

Recent investigation of the relationship of preliminary treatment to mortality following prostatectomy has definitely established the necessity of preliminary treatment in all cases.

Hunt believes that in 75 per cent of cases prostatectomy can safely be performed by the one-stage visualized operation, which permits the application of the general principles of surgery, that is, exposure, accuracy of conduct and complete hemostasis. He emphasizes the importance of avoiding anesthesia by inhalation, and of using the various forms of local anesthesia. The advantages of the one-stage over the two-stage operation are also dealt with, and the operation is illustrated.

The discussion of mortality in this paper is based on a five year period, during which time suprapubic prostatectomy was performed on 995 patients at the Mayo Clinic.

This series has been carefully reviewed with regard to the mortality rate, subsequent course and ultimate function. In several series of cases of 100 each, there were no deaths. The mortality rate by years, however, has varied from 6.4 per cent in one year to 2.4 per cent in 1925, with an average rate of 4.2 per cent for the five year period. In this connection, it should be stated that previous to January, 1925, preoperative preparation was carried out in only about 75 per cent of the cases. The remaining 25 per cent of the patients were in excellent general condition and were operated on without preoperative preparation. The effect of preoperative preparation in all cases after January, 1925, became apparent immediately.

The one-stage operation was performed in 783 cases (78.6 per cent) of the series with 34 deaths, a mortality rate of 4.3 per cent. In 212 cases, the two-stage operation was performed with 8 deaths, a mortality rate of 3.7 per cent. This is in contrast with a previous report on an earlier series of cases in which the mortality rate of the two-stage operation was one and a half times as high as that for the one-stage operation.

ble. Before the sutures are tied, the metal catheter is replaced by a silk one which is retained for twelve or fourteen days after operation. A drainage tube is placed in the opening of the prostatic capsule, which is partially closed by means of a single suture. Packing is not inserted. The superficial part of the wound is brought together by a few sutures. As a rule, the wound heals by primary intention. The perineal drainage tube is removed three or four days after operation, and the fistula heals so quickly that the catheter can be removed in from ten to fourteen days. The patient is then able to pass urine normally through the urethra.

The main points in which this method differs from other perineal operations are: (1) complete resection of the part of the prostatic urethra encircled by the adenoma, (2) suture of the neck of the bladder to the urethral stump, and (3) suture of the incised prostatic capsule.

This method of prostatectomy causes only slight injury to the tissue. Little blood is lost, and serious postoperative hemorrhage rarely occurs. Infection rarely follows perineal prostatectomy, the wound is smooth, there are no cavities or flaps of necrotic tissue, and the area is well drained.

Mortality after perineal prostatectomy is lower than after suprapubic. Wildbolz reports a mortality of 15 per cent in 105 suprapubic operations in contrast to a mortality of only 6.5 per cent in 305 perineal operations. In 29 of Wildbolz' cases, healing of the perineal fistula was delayed. In 1 case, the fistula persisted for more than three months. In 3 cases, there was a persistent urethrorectal fistula which required another operation for relief. Partial incontinence lasting for a few weeks was observed in 6 cases, and in 5 others it persisted for more than four months.

In discussing indications for prostatectomy, Hunt<sup>34</sup> says that inability to empty the bladder and persisting residual urine are the outstanding and important indications for prostatectomy. The absence of residual urine, however, does not constitute contraindication to operation if the gland is enlarged and there are subjective symptoms. With any amount of residual urine as a result of prostatic obstruction, the indications for operation are clear; with frequency, difficulty, pain and other symptoms, but with slight enlargement of the gland and no residual urine, the advisability of operation is questionable.

Death following prostatectomy has been due to the following causes, in order of frequency: (1) coexisting or preexisting cardiovascular, renal and pulmonary diseases; (2) surgical accidents, such as hemorrhage, and (3) postoperative complications. In recent years, effort has been directed toward providing factors of safety which tend to eliminate

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34. Hunt, V. C.: Immediate and End Results of Suprapubic Prostatectomy. A Consideration of the Factors Involved, *Canad. M. A. J.* 17:1467, 1927

the orifice, and the tampon is removed by pulling gently on the thread emerging from the wound. In removing the tampon, the coils of Penrose tubing are gently manipulated, and these tend to unfold themselves, leading to little discomfort.

[ED. NOTE.—The use of coiled Penrose tubing as a tampon is perhaps a new feature. One can imagine that it would be difficult in all cases to get such a tampon to fit snugly enough for hemostasis at all points of the capsule. The pull of a thread through the urethra also would possibly be associated at times with cutting into the urethral tissue at the region of the bulb or triangular ligament and might call for a considerable amount of adjustment. The principle of counterweight traction is not without virtue, although the attachment of the weight to a Hagner-Pilcher bag would seem more likely to produce less discomfort, hemostasis would be better because of more uniform contact of the bag with the prostatic capsule, and the removal of the bag might be more certain and less difficult as a rule than that of coils of Penrose tubing. Any type of persistent pull on the remaining muscles at the neck of the bladder tends to increase the possibility of transient incontinence. The system of weights suggested by Ware would at least offer consistent tension and be free from the irregularly strong and weak tension occurring when the urethral tube of the hemostatic bags is attached to the patient.]

Thomas <sup>36</sup> states that according to estimates, 50 per cent of patients with prostatic disease die within five years after the onset of obstruction, and that catheter life shortens this to two and a half years.

The function of the kidney is one of the most important factors in determining the qualifications of a patient for operation. An estimation of the urea nitrogen in the blood and the quantitative percentage output of phenolsulphonphthalein are the most commonly used tests of renal function. Normal values of urea nitrogen in the blood range from 12 to 20 mg. per hundred cubic centimeters; safe values range from 20 to 30 mg.; values of above 30 mg. should be regarded as dangerous, if not prohibitive of operation. The cardiovascular system and the blood are next to renal function in importance. As a result of the study on the cause of death following prostatectomy, Thomas notes the following rules: In cases in which low tension is present, when the systolic blood pressure is 110 or less, the diastolic must be more than 60; if the diastolic pressure is less than 60, the systolic must be more than 110. In cases in which high tension is present, when the systolic pressure is 180 or more, the diastolic must be less than 100; if the diastolic pressure is more than 100, the systolic must not be more than

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36. Thomas, B. A.: *Vital Factors in the Management of Prostatic Obstruction*. Ann. Surg. 86:563, 1927.

The causes of the 42 deaths were as follows: uremia and renal insufficiency, 10; pulmonary embolism, 9; general sepsis, 7; cardiovascular disease, 6; secondary bleeding, 4; pneumonia, 3, and bleeding duodenal ulcer, general peritonitis, and erysipelas, 1 each. Renal insufficiency and uremia are important factors in cases in which urinary obstruction and retention have existed for a long time. Pulmonary embolism has not occurred as a cause of death since the adoption of preoperative preparation of all patients. It has continued to be difficult to combat general sepsis, which usually emanates from an acute exacerbation of cysto-ureteropyelonephritis. It would seem that prostatectomy had little to do with some of the deaths, but these deaths are included in the surgical mortality.

The late results were good. The preoperative difficulty in urination was relieved in 95 per cent of the patients.

Ware<sup>35</sup> condemns the packing of the prostatic capsule with gauze tampons, as ineffective and cumbersome. The Hagner and Pilcher bags overcome the disadvantages of gauze tampons, but these bags come in contact with the prostatic bed by drawing taut the rubber tube at its exit from the urethra and maintaining this pull by anchorage to a cradle with its points of support on the pelvis. These cradles are at times difficult to adjust and hamper the movements of the patient. Ware has devised a method which he believes is superior. On completion of enucleation, a Nélaton catheter is introduced until the vesical end becomes visible or can be palpated. A length of water-proofed linen fishing line is secured to the vesical end drawn into the wound. The catheter is withdrawn until a length of thread emerges which passes over a pulley at the foot of the bed and reaches the floor. Some Penrose tubing is secured to the thread emerging from the abdominovesical wound by throwing a knot about loosely coiled folds of the tubing arranged in roset fashion, or with greater refinement transfixing loops of tubing with the same thread armed with a large needle. When this is accomplished, the thread coursing through the urethra is pulled on, causing the rubber tampon to follow until the resistance of the prostatic bed at the introitus of the bladder is felt. Traction is sustained by applying a sand bag weighing from 3 to 5 pounds (1.4 to 2.3 Kg.) to the end of the thread, which is allowed to fall over the end of the operating table. When the patient is put to bed, the end of the thread, with its weight, plays over a pulley. The weight may be adjusted to the comfort of the patient. A thread attached to the tampon is allowed to emerge from the suprapubic wound at the time of closure.

In from forty-eight to seventy-two hours, when the need for hemostasis is past, the thread emerging from the urethra is cut close to

35. Ware, M. W.: Sustained Counterweight-Traction in Hemostasis of Prostatectomy. *Ann. Surg.* 86:561, 1927.

There is a marked and rapid increase in the volume of the gland. The diagnosis is frequently confused with that of carcinoma of the prostate. A single lump on the surface of the prostate usually means the onset of malignancy. Numerous irregularities and lumps suggest prostatitis. Pus in the expressed prostatic secretion and the presence of eosinophilia help confirm a diagnosis of infection.

It is easier to make a diagnosis in acute cases, and these are more significant on account of the urgency of treatment. Prostatectomy is the procedure to be used, preferably in two stages. In acute forms, however, when the condition of the patient does not permit delaying operation, perineotomy must be performed to permit evacuation of the pus. At the same time, the bladder should be drained.

Casariago<sup>39</sup> advises perineal prostatotomy as the treatment for patients with urinary retention due to acute gonorrheal prostatitis; the posterior surface of the prostate is exposed by means of a deep longitudinal incision over both lobes. Persistence of retention of urine in a case of acute gonorrheal prostatitis is a sign of formation of abscess with more or less destruction of the gland. Prostatotomy avoids this and prevents the formation of caverns and fistulas of the prostate. It may often be considered as prophylactic treatment of chronic prostatitis.

*Calculi.*—Thomas and Robert<sup>40</sup> give an extensive review of the literature on prostatic calculi and report three cases. Although cases have been reported occasionally in the older literature, it usually was not considered that the stones originated in the gland itself. In more recent times, however, prostatic calculi have ceased to be a rarity; they are, in fact, much commoner than the number of reported cases would indicate. The etiologic factor of true prostatic calculi is still hypothetical. These calculi, whether septic or aseptic, have as a nucleus the corpora amylacea, which are albuminoid or nitrogenous-like bodies. They are usually multiple and the size of a "millet seed" or a "pea"; they are most common in middle and late life and are associated with other pathologic conditions. About 65 per cent do not cause symptoms and are found accidentally during routine roentgen-ray examination or at operation. A persistent and rebellious prostatitis should arouse suspicion of calculi. Serious sequelae, such as abscess and gangrene, are rare. Malignancy and inflammatory nodules can be differentiated in almost 100 per cent of cases by means of roentgenograms. Phleboliths must be taken into consideration. Surgical intervention by the perineal route is the procedure of choice, except in cases in which the calculus communicates with the urethra, when it may be removed through the urethroscope.

39. Casariago, A. G.: Prostatotomy as Treatment of Urinary Retention Due to Acute Gonorrheal Prostatitis, *J. Urol.* 18:401, 1927.

40. Thomas, B. A., and Robert, J. T.: Prostatic Calculi, *J. Urol.* 18:470, 1927.

175. This is not so-called "pulse pressure" in its usual sense, but rather pulse pressure with systolic and diastolic limitations. Thomas has performed operations successfully in cases in which the systolic pressure was less than 110, or even 100, but the diastolic was always more than 60; conversely, he has had cases in which the diastolic pressure was less than 60, but the systolic was always more than 110. On the other hand, if the systolic pressure is more than 190, operation is a hazardous procedure, but it has been performed successfully several times when the diastolic pressure was less than 100; conversely, in many cases in which the diastolic pressure was as high as 120, prostatectomy has been performed with recovery, but the systolic pressure was invariably less than 175.

Age, in itself, is never a vital factor in prohibiting operation on the prostate. Thomas believes that it is unwise to force old men out of bed too soon. The many complications incident to epididymitis, to phlebitis and to embolism will thereby be averted.

Lowsley and Harrah<sup>37</sup> report a case of complete retention of urine in a man, aged 32, due to solid tumefaction of the prostate gland. Suprapubic cystostomy was performed.

The patient was subjected to suprapubic cystotomy under local anesthesia. Examination of the interior of the bladder revealed a rather firm mass about 4 cm. in diameter, extending from the floor of the neck of the bladder. A specimen was taken from this tumor-like projection and sent to the laboratory for examination. The bladder was drained by suprapubic suction for a period of fourteen days, after which the prostate was removed suprapubically under sacral and parasacral and regional anesthesia.

The growth had greatly increased in size since the first operation. Microscopic examination showed chronic inflammation suggestive of Hodgkin's lymphogranuloma.

*Prostatitis.*—Le Roy<sup>38</sup> reviews a series of thirty-four cases of suppuration in prostatic hypertrophy. He believes that these conditions are relatively common and often pass unnoticed, because at times the pain is only moderate, and pyuria, the patient's general condition, and the absence of unusual symptoms are not suggestive of the principal disease. Prostatic suppuration calls for energetic and immediate treatment; otherwise serious complications set in.

The urine is often clear, and, unless a rectal examination is made, the diagnosis may not be apparent until the condition is far advanced. The patient complains of a heavy feeling in the perineum and dysuria.

37. Lowsley, O. S., and Harrah, F. W.: Enlargement of the Prostate Gland with Characteristics Resembling Hodgkins' Disease, *Ann. Surg.* **86**:559, 1927.

38. Le Roy, C. M.: Des suppurations locales dans l'hypertrophie de la prostate. *J. d'urolog. méd. et chir.* **23**:311, 1927; **23**:388, 1927.



Schüppel<sup>42</sup> states that cystitis gangraenosa desiccans is the most unfavorable form of inflammatory disease of the bladder. The name was given to this disease by Stöckel, who first described it and reported two cases. Although it is not possible to determine the number of reported cases, many have been observed.

The prognosis is grave. In Subotski's 167 cases, there were 90 deaths. Constantini reports 18 (40 per cent) deaths in a group of 45 women and 17 (51.5 per cent) in a group of 33 men. Houltani reports 8 (24.2 per cent) deaths among 33 pregnant women. This high mortality in women is explained by the association of this condition with unsuccessful abortion and adherent retroflexed uterus. The lower death rate among women in general is due to the fact that the urethra is shorter and permits more satisfactory drainage of the bladder. In men, prostatic disease, urethral stricture and tabes dorsalis are responsible for most of the deaths.

Successful treatment depends on an early diagnosis, which necessitates a study of the underlying causes. Frönstein classifies the cases into four groups:

1. The destructive factor began with some type of chemical which had been introduced into the bladder in too strong a concentration. In one case the condition was brought on by the introduction of 100 cc. of 20 per cent potassium permanganate, in another by the injection of 10 per cent sodium bromide for cystography.

2. In this group, the condition was caused by external pressure, such as retroflexion of the uterus, and urinary retention due to urethral stricture and prostatic hypertrophy.

3. The infectious cystitis had existed for a long time and gradually changed to a gangrenous type without mechanical factors.

4. In this group, the condition followed diphtheria, roentgen-ray therapy, impaction of calculus in the urethra, and extension from inflamed appendix.

The best treatment is the establishment of free drainage, following cystotomy. Any urinary obstructions should be relieved. Many cases go on to the stage of contracted bladder with consequent infected ureterohydronephrosis. Occasionally, the contraction of the bladder is so marked that help is obtained only by plastic operations. Schüppel cites a case in which there were multiple urethral strictures.

*Decompression.*—Bonneau<sup>43</sup> states that in the presence of marked distention of the bladder in patients who have not been catheterized and

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42. Schüppel, A.: Ueber cystitis gangraenosa dissecans und die Therapie ihrer Folgen, Arch. klin. Chir. 145:380, 1927.

43. Bonneau, M. R.: Evacuation lente de la vessie par drainage sus-pubien filiforme avant la cystostomie, Presse méd. 2:1350, 1927.

## BLADDER

**Gangrene.**—Carson<sup>41</sup> reviews 167 cases of necrosis and gangrene of the urinary bladder noted in the literature and added 6 cases in which necropsy was performed at the University of Maryland. Necrosis or gangrene of the bladder occurs as a result of: (1) interference with the circulation, internal or external pressure; (2) infection, general or local, with or without mechanical injury; (3) lesions of the central nervous system, and (4) chemical irritants.

There were 116 females and 57 males. The age varied from 3 to 75 years, the majority of patients being in the third and fourth decades.

Of the 173 patients, 102 died, 67 recovered and 4 were not traced. In 40 cases, the gangrene occurred in pregnant women; in 23 it occurred after labor; in 15 it was associated with retention of urine; in 11 females it was due to external pressure with retention in 6. Cystitis was the antecedent in 14 cases (7 males and 7 females). The cystitis was complicated by retention in 7 of the 14 cases by stricture of the male urethra in 9 cases, in which there were calculi in the urethra in 3. In 6 cases prostatic obstruction with retention was present, in 6 calculi in the bladder with retention, and in 6 irritants were a factor and retention was associated. General infections played a part in 15 cases, in 7 of which there was retention. In 12 cases there were lesions of the central nervous system, retention being present in 7. Trauma was the cause in 5 cases; retention was associated in 3 of these. Extroversion of the bladder through the urethra occurred in 5 cases. There were 20 miscellaneous cases, retention being an added factor in 10 of these. In all, retention was present in 76 (48.5 per cent).

Obstruction of the circulation will explain the cases of simple necrosis, but pathogenic bacteria must be present before putrefaction can take place.

In the 67 cases in which the patients recovered, the diagnosis was made by cystoscopic examination, suprapubic cystotomy or examination of the exudate passed by urethra.

At necropsy, the mucosa of the bladder was frequently found to be yellowish, greenish yellow, or black with a putrefactive odor, and the perivesicular tissues showed evidences of varying degrees of inflammatory reaction, trigonitis, peritonitis and ureteritis.

[**ED. NOTE.**—In view of the clinical rarity of gangrene of the bladder, Carson's excellent review is timely. From a pathologic standpoint, regardless of the exciting factor, one must feel that ultimate interference with the vesical blood supply to such an extent as to destroy nutrition is the real cause of the condition. This presupposes a fulminating infection, intense irritation, or severe trauma, as is borne out by the cases reported.]

41. Carson, W. J.: Gangrene of the Bladder, *Ann. Surg.* 85:200, 1927

In this way, the necrosis and bleeding can be cleared up and the tumor reduced in size sufficiently to allow further treatment with electrocoagulation.

According to experiments on animals carried out by Drexler and Ginberg, chemocoagulation apparently does not have any permanent injurious effect on the normal mucosa of the bladder.

*Ulceration.*—Dean <sup>45</sup> reports three cases of ulceration of the bladder, a late effect of applications of radium to the uterus. These cases are usually seen by urologists, and the symptoms and appearance suggest carcinoma of the bladder, but a tumor is not present.

There is often a history of irradiation with radium to a nearby organ, and there is an area of necrosis at the site nearest the application of radium. A histologic section is at times necessary to rule out a diagnosis of carcinoma or tuberculosis. There is an interval of at least a year between the time of the irradiation and the onset of symptoms.

The distressing subjective symptoms have been relieved readily by a prescription consisting of sodium citrate, 20 Gm., tincture of hyoscyamus, 25 cc., and enough cinnamon water to make 120 cc., given 1 teaspoonful in water two hours after each meal.

The most satisfactory treatment for the lesion consists of injections of mercurochrome-220 soluble into the empty bladder. To prevent undue irritation, the earlier instillations consist of 15 cc. of a 1:200 dilution, administered three times a week. Later, when healing results in greater toleration, the strength of the solution may be increased gradually to 2 per cent, the same quantity being used as before at the same time intervals. It is important that this treatment be carried on with regularity and persistence.

[ED. NOTE.—In some cases, it is almost impossible to distinguish between radium irritation, ulceration or malignancy of the bladder, especially in cases in which radium has been applied for primary tumor of the bladder. The area in the bladder is usually reddened, raised and edematous, and has all the appearances of a primary lesion of the bladder. Another point is that brought out by Dean in this paper that there are sometimes intervals of at least a year between irradiation and the onset of the symptoms.]

*Exstrophy.*—Colby <sup>46</sup> reports a case of exstrophy of the bladder in a boy, aged 7. At one operation the left ureter was isolated from the bladder and transplanted to the sigmoid. Three weeks later at a second operation, the right ureter was transplanted to the cecum; it was neces-

45. Dean, A. L.: Ulceration of Urinary Bladder as Late Effect of Radium Applications to Uterus, *J. A. M. A.* 89:1121 (Oct. 1) 1927.

46. Colby, F. H.: Exstrophy of Bladder; Report of Case, *Boston M. & S. J.* 96:1033, 1927.

whose urine is normal, slow decompression of the bladder is of great advantage; he empties the bladder by means of a lumbar puncture needle of small caliber, introduced into the bladder suprapubically. The bladder is usually completely evacuated in twelve hours. The urinary equilibrium is reestablished, and secondary cystostomy may be carried out without risk to the patient.

Perrier, in discussing Bonneau's paper, states that he also makes a suprapubic capillary puncture in cases of marked distention. He reports a case in which this procedure was carried out on two occasions; the second was necessary on account of too long a delay before proceeding with the cystostomy.

Gerard, in cases of extreme distention, makes a small button-hole incision in the bladder through which he inserts a small catheter which is opened intermittently every other hour, permitting 200 cc. of urine to escape. The catheter is permitted to drain continuously after the fourth day.

[ED. NOTE—All stab or punch operations through the suprapubic region carry a moderate risk on account of possibility of injury to the peritoneum and urinary extravasation. The same results as those obtained by Bonneau can be carried out by various methods of decompression with a urethral catheter, notably that described by Foulds and Bumpus.]

**Tumors.**—Drexler and Ginberg<sup>44</sup> state that during the last eight years Joseph has treated more than fifty patients with benign and malignant tumors of the bladder either by chemocoagulation alone or by chemocoagulation combined with electrocoagulation. The technic is as follows: A cystoscope is passed and the bladder washed and filled as for cystoscopic procedure. A ureteral catheter with an open end is inserted through the cystoscope, and from 20 to 30 drops of freshly prepared solution of trichloroacetic acid is run over the upper surface of the tumor. The tumor becomes white due to action of the acid. After treatment the bladder is emptied and washed.

Patients with tumors situated in an area of the bladder inaccessible to the cystoscope can be treated with frequent instillations into the bladder of from 40 to 50 cc. of distilled water containing from 20 to 30 drops of trichloroacetic acid. Long-standing hematuria, the result of tumors of the bladder, can also be arrested in this manner. After two or three weeks either the tumor entirely disappears and is replaced by scar tissue, or it is reduced in size and is ready for further treatment.

Chemocoagulation is especially indicated in cases of carcinoma of the bladder with foul-smelling necrosis and bleeding with secondary cystitis.

44. Drexler, I. S., and Ginberg, W.: Treatment of Bladder Tumors by Chemocoagulation. *Surge, Gynec. & Obst.* 45:820, 1927.

[ED. NOTE.—Torsion of the cord is so frequently associated with descended or partly descended testes in which some developmental error is present that it is interesting to note the occurrence of the condition in the abdomen. Thus another infrequent type of lesion must be considered in the differential diagnosis of disease of the lower right quadrant. The absence of the testis from the scrotum might point to such a lesion if other features of the condition are not contradictory.]

*Tumor.*—Roeder <sup>48</sup> describes a case of hyperplasia of the subperitoneal fat beneath the mesothelial coat (tunica vaginalis viscerum) of the testis. The patient had a left indirect inguinal hernia with a hydrocele of the tunica vaginalis. At operation, surrounding the cord and beneath the sac, was a continuous and complete layer of fat extending from the testis up to and through the internal inguinal ring. After the sac of hydrocele had been dissected away, a small nodule beneath the testicular layer of the tunica vaginalis was noted. This proved to be a lipoma, well encapsulated, and more intimately attached to the tunica vaginalis than to the tunica albuginea.

In reviewing the literature, attention is called to the fact that the scrotum embryologically is formed by a constriction of the walls of the lower part of the abdomen. The constriction includes the peritoneum and subperitoneal areolar tissue, the presence of which naturally favors the deposition of fat. Therefore, so-called fatty tumors of the testis should be regarded as hyperplasia of the subperitoneal fat originating from the areolar tissue beneath the tunica vaginalis viscerum or the testicular peritoneum. To be carefully differentiated, are masses of fat along the mesothelial tunics of the cord and fatty tumors in the region of the inguinal canal. Eight cases of lipoma of the testis are reported from the literature and analyzed. In the majority of these the tumor probably originated from the lower end of the cord and therefore cannot be classified as true testicular tumor, by the foregoing criteria.

[ED. NOTE.—In differentiating scrotal tumors one seldom thinks of the possibility of lipoma, a lesion which occurs surprisingly at times in other parts of the body. Roeder calls attention to the embryologic occurrence of this tissue in the scrotal contents and the clinical possibility of encountering such cases should be borne in mind.]

*Infarction.*—Lubash <sup>49</sup> reports a case of infarction in the testis. The testis belongs to the same category as the kidney, spleen and brain, in that its circulation is terminal. Since infarction of the testis exists, it should be thought of as an entity.

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48. Roeder, C. A.: Lipoma of the Testicle, *Ann. Surg.* 85:275, 1927.

49. Lubash, Samuel: Infarction of the Testicle, *J. Urol.* 18:421, 1927.

sary to use the cecum to receive this ureter to avoid tension. Photomicrographs of the tissue removed from the bladder showed numerous mucus-secreting glands.

[ED. NOTE.—The mucus-secreting surface, described by Colby, is common in most cases of exstrophy of the bladder; it is the result either of metaplasia of the normal covering or of hyperplasia of glands in the mucosa. Such glandular structure often shows characteristics of malignancy.]

#### TESTIS

*Torsion.*—Ormond<sup>47</sup> states that about 150 cases of torsion of the spermatic cord are on record, the first case having been reported by Delasiuave in 1840. It occurs most often near the age of puberty, although a few cases are reported shortly after birth and a few at 60 years or more. The condition has also been observed at birth. The right side is slightly more affected than the left. Developmental errors most often associated with undescended testes (52 to 69 per cent of cases) have been held to be a predisposing cause.

Etiologic factors mentioned are an abnormally loose scrotum, a voluminous tunica vaginalis, an unusually long gubernaculum, and an abnormal attachment of the cord to the testis. From a consideration of the anatomy, Ormond holds that the last two are the most probable etiologic factors. Ordinarily, the reflection of the parietal layer of the tunica over the epididymis forms a mesentery running from the globus minor up to the middle of the globus major. In most of the recorded cases of torsion, this has been much shortened and includes only the globus major, and the twist occurs in this very much shortened mesentery.

Ormond notes in the literature five cases of torsion in intra-abdominal testis and adds a case of his own, that of a man, aged 42, who had experienced intermittent right-sided abdominal pain for two days before admission. At operation a mass was found consisting of a black swollen testis, with one complete twist of its mesentery, the testis being adherent to the tip of the appendix. There was no evidence of malignancy, which had been noted in three cases in the literature. In only one case (Stiles) was preoperative diagnosis definitely determined.

In all these cases, the testis was on the right side. This is not true of torsion generally, although the right side is more frequently affected than the left, just as it is in maldescent of the testis, which seems to be the chief etiologic factor in torsion.

Ormond hypothesizes that torsion in the intra-abdominal testis may be found usually on the right side because of the presence of the cecum with its intermittent loading and pull on the peritoneum.

47. Ormond, J. K.: Torsion of an Intra-Abdominal Testis, *Ann. Surg.* 85:280, 1927.

Stricture of the ureter was seen in ten patients, three boys and seven girls. Diverticula and tumors of the bladder were also encountered.

It is shown that the urinary diseases of childhood resemble those of adult life, and that with practice, cystoscopy in children can be accomplished without difficulty, and may be useful for therapeutic procedure as well as for diagnosis.

Hunter and Montgomery<sup>52</sup> follow up the work of Andrewes, who, when investigating the hypobilirubinemia indicated by the van den Bergh test in uremic serum, discovered a new type of diazo-reaction. On allowing the mixture of alcoholic extract from a uremic serum to stand in contact with the van den Bergh reagent for a period of twenty-four hours, Andrewes found that a pinkish-brown or buff color developed, and that when this was made alkaline with a strong alkali, a bright red color appeared immediately; this was stable for from a few minutes to more than half an hour according to its original intensity.

Hunter and Montgomery observed nephrectomized rabbits and dogs, and thus confirmed the work of Andrewes. As a result of their investigations, they modified the technic previously used and presented the following:

One gram of sulphanilic acid is added to a liter flask containing about 500 cc. of water and 15 cc. of 37 per cent (concentrated) hydrochloric acid. The contents are shaken at ordinary temperature till the sulphanilic acid has gone into solution. Water is then added and the contents mixed. The solution keeps indefinitely.

It is more convenient and reliable to have a stock 5 per cent solution of sodium nitrite than to make 0.5 per cent solutions at weekly intervals. Five grams of good quality sodium nitrite is dissolved in 100 cc. of water. This, if kept in a stoppered bottle in an icebox, is reliable for at least a year, and for several months without the latter precaution. One cubic centimeter of this solution is mixed with 9 cc. of water before each diazotization.

The test is performed by precipitating and centrifugalizing the serum or plasma with 2 volumes of 95 per cent alcohol, taking 1 cc. of the supernatant fluid in a small test tube, adding 0.4 cc. of the diazo-reagent and 0.1 cc. of concentrated hydrochloric acid. The tube is heated over a flame or in a water bath at about 80 C., for a minimum of two minutes. If the test is positive, the buff color will then have developed fully. The tube is cooled and 1 cc. of 2.5 normal solution of sodium hydroxide is added and the tube quickly inverted. The intensity of the red color thus produced accords with the buff color obtained in the acid solution. As the buff color is stable, it is the more suited for

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52. Hunter, George, and Montgomery, R. C.: On the Diazo Reaction in Uremic Serum and in Normal Urine, *Canad. M. A. J.* 17:148, 1927.

The etiology, although still obscure, may be classified as follows: (1) predisposing, any condition that could cause embolism; (2) exciting, a temporary twist of the cord that may result in stasis in one of the arterioles. Infarction of testicle should be suspected in patients with temporary torsion whose symptoms return after abatement. The treatment is purely surgical in the form of orchidectomy.

#### URETHRA

Chauvin<sup>50</sup> distinguishes four groups of double urethra: 1. The complete double urethras which are more or less permeable canals extending from the bladder to a definite meatus; there is no connection between the two urethras. 2. The one-eyed juxtra-urethral ducts, which end in a culdesac at one or the other of the extremities open either into the bladder or to the exterior. 3. The bifurcation type of unique, and it is the anterior segment which bifurcates into two portions. At times the deep urethra is unique, and it is the anterior segment which bifurcates into two portions. In other cases the reverse disposition, in which the anterior is single and the posterior portion is double, is found. The accessory canal in this form may be on top, underneath or on the side of the principal urethra. 4. The fourth type comprises the canaliculized diverticula; they communicate by one of their extremities. In this type are merely small cellules which usually dip down into the spongy or prostatic urethra.

#### UROLOGIC DIAGNOSIS

Kretschmer<sup>51</sup> points out that all adult patients who present symptoms of lesions in the genito-urinary tract are generally subjected to a complete urologic examination. This is not ordinarily the case with children, although infants and children are subject to almost all the urologic diseases of adult life, except enlargement of the prostate and carcinoma. As a matter of fact, small children can be subjected to a complete urologic examination. There are seven patients in this series under 12 months of age. The youngest was a boy, aged 27 days. Thirty-four of the patients were males and fifty-two were females.

The symptoms in children and adults are about the same in order of incidence: fever, pain, cloudy urine, frequency and hematuria.

In disorders of the kidney, pyelitis leads the list, followed by tuberculosis. The patients with persistent pyelitis were treated by pelvic lavage with solutions of silver nitrate.

50. Chauvin, E.: À propos des urètres doubles; en particulier de leurs variétés postérieures, *J. d'urolog. méd. et chir.* 23:289, 1927.

51. Kretschmer, H. L.: Urologic Problems in Infancy and Childhood, *J. Urol.* 18:433, 1927.



All cases of spontaneous cystitis, all cystitis resisting the usual treatment for this condition and recurring cases of cystitis suggest tuberculosis. In all cases of cystitis, except those following urethritis, cystoscopy should be carried out. Catheterization of the urethra should not be preceded by a general examination of the bladder. Any type of hematuria demands immediate urologic examination.

All patients with renal pyuria which is not definitely tuberculous require roentgen-ray examination. All roentgen-ray examination for renal stone should include the entire urinary tract.

The use of vaccines is often a "cache-misère," masking the physician's ignorance and his incapability of establishing a diagnosis of infection. The diagnosis should be made primarily, and vaccine should never be used unless other methods are useless.

Marion,<sup>55</sup> in discussing the value of phenolsulphonphthalein, insists on the following points: 1. One should always use phenolsulphonphthalein of the same origin. 2. In an intravenous injection, it is necessary that the entire amount be injected into the vein. 3. The measure of standard must be frequently renewed. 4. If the result is doubtful, the test must be repeated several times.

A patient eliminating large quantities of phenolsulphonphthalein can usually be considered as having good resistance. In cases in which the amount of phenolsulphonphthalein is found low on several occasions, the surgical outlook is usually poor.

The phenolsulphonphthalein test is more reliable than the so-called Ambard's "constant"; if fever is present, the constant improves, whereas the amount of phenolsulphonphthalein eliminated diminishes, giving a more accurate index of the condition.

Pescatori<sup>56</sup> cites a case which he called "false appendicitis." The patient had pain in the right hypochondrium, radiating into the ileocecal fossa and occasionally to the left side. A diagnosis of chronic appendicitis was made, but roentgenologic examination revealed a "bean-sized" stone in the left kidney. Roentgenograms of the gastro-intestinal tract were negative. Removal of the stone was followed by uneventful recovery. Pescatori calls attention to this case, and it is cited here to show the valuable use of the roentgen ray in differential diagnosis, a point in technic used in American urologic circles for a long time.

[ED. NOTE.—This report is of interest in that the clinical course is the opposite to that usually observed. Frequently, patients with urinary calculi are subjected to one or more abdominal operations before the true nature of their condition is determined. In a series of more than

55. Marion, G.: À propos de l'épreuve de la phénosulfophthaléine, *J. d'urolog. méd. et chir.* 24:57, 1927.

56. Pescatori, Guido: Sindrome appendicitea da calcolosi renale sinistra rivelatasi ai raggi X, *abstr. Ztschr. f. urol. Chir.* 21:13, 1926-1927,

comparative tests. At any rate, it can be preserved until it is convenient to add alkali to a series of tubes at one time.

As originally pointed out by Andrewes, the secondary red color is produced only by the addition of strong alkali. This color will not develop with strong alkali in the presence of a large amount of ammonia, so that ammonium sulphate cannot be used in this test in association with alcohol to precipitate the proteins from the serum, as recommended by Thannhauser and Andersen for the van den Bergh test.

Their technic makes the test more sensitive and renders it less subject to interference. The substance giving the diazo-test in uremic serum is shown to be a normal, but as yet unidentified, urinary constituent.

Gottlieb and Strokoff<sup>53</sup> report several cases in which pneumopyelography was employed. They drew the following conclusions from their study: 1. This is a method of choice on account of the absence of irritation even in cases of hydronephrosis. 2. It permits the obtaining of pictures of stones which are not usually opaque in roentgenograms. 3. Only one roentgenogram, instead of two, is necessary to make the diagnosis. 4. Its technical application is simple and harmless when properly used.

[ED. NOTE.—Pneumopyelography has not been used extensively in this country. Apparently from reports in American periodicals the results are not so successful as reports from foreign clinics seem to indicate. As cystoscopy and pyelography are such satisfactory diagnostic procedures, and in most cases permit a precise diagnosis, pneumopyelography would have to be markedly improved before it is used to any extent in American clinics.]

Marion<sup>54</sup> gives a number of general principles in diagnosis and treatment of urologic conditions. He states that it is necessary to establish the diagnosis of a disease by relying on one physical symptom, such as pyuria or hematuria, rather than on a functional trouble, such as pain or frequent urination.

If, during urethral catheterization, obstruction is encountered in the region of the bulb of the urethra, a Béniqué catheter should be used and not a sound or a bougie of smaller caliber.

Hematuria in a patient with prostatic hypertrophy must not be attributed to the prostatic enlargement unless all other causes of hematuria have been eliminated.

A patient suffering from chronic urinary distention caused by prostatic hypertrophy should not be catheterized; the bladder should be drained and explored.

53. Gottlieb, J. G., and Strokoff, F. J.: *La pneumopyélographie*, J. d'urol. méd. et chir. 23:328, 1927.

54. Marion, G.: *Quelques grands principes directeurs du diagnostic et de la thérapeutique urologiques*, J. d'urol. méd. et chir. 23:194, 1927.

A choice is given of nitrous oxide, ethylene, spinal anesthesia, sacral block and local infiltration. Spinal anesthesia is disapproved because of its effect on the blood pressure, preference being given to sacral block and local infiltration, for suprapubic and scrotal operations and to regional block, local infiltration and analgesia by nitrous oxide oxygen for operations on the kidneys, at times to be supplemented with local infiltration.

In operations on the bladder and prostate, sacral block, combined with infiltration of the abdominal wall, is recommended, the technic of Hunt being followed. The wall of the bladder is also infiltrated, as well as the capsule of the prostate, if this is the point of attack. Usually this procedure will suffice, but the anesthetist must reassure the patient; if there is apprehension, he should be ready to administer nitrous oxide to the point of analgesia. The patient is for this reason given a preliminary hypodermic injection of morphine and atropine.

In the genito-urinary examining room, Lower prefers the use of procaine to cocaine as a urethral anesthetic, especially in operations such as urethrotomy. For cystoscopy 10 cc. of a 2 to 4 per cent solution of procaine is used. If a pyelogram is to be made, morphine is not given, as Lower believes that the patient should be sensitive to the pain of renal distention. In cases of tuberculosis of the bladder, sacral anesthesia finds a field of usefulness. It is contraindicated in punch operations because of the fact that complete relaxation of the neck of the bladder frequently follows sacral block. Local infiltration of the neck of the bladder, together with analgesia by nitrous oxide, finds a field of usefulness here.

In the case of old men with enlarged prostates, the combination of sacral block and abdominal wall infiltration is emphasized as being a life-saving procedure.

[ED. NOTE.—Lower expresses the thought of the more progressive urologists of the day. Sacral block is easily administered in the average case, and with infiltration of the abdominal wall as a rule no further injection of the bladder or prostate itself will be needed. If the anesthesia is properly administered, it may be said also that pain will as a rule be absent, and there will seldom be need for nitrous oxide or any form of anesthesia by inhalation unless it is given because of apprehension or mental confusion of the patient. Lower uses procaine as an anesthetic for the urethral mucosa. It has been the experience of most urologists that procaine has little surface action; in order to have an anesthesia with a satisfactory surface action, it is usually necessary to use cocaine.]

1,400 patients with renal stone, 50 per cent had had at least one operation and 20 per cent, two or more operations before the renal stone was removed. In a second series of 400 cases of ureteral calculi, either the gallbladder or the appendix had been removed in 23 per cent. In at least half of these cases, stones had been present in the left ureter.]

Jeck and Munch<sup>57</sup> point out the truth of the words of Watson, who says: "In the examination of urine for tubercle bacilli, the method which requires the fewer laboratory reagents, consumes less time, and gives a higher percentage of positive results is the one which will be used eventually." They, therefore, carried out a most thorough and convincing group of experiments, proving the value of simple centrifugalization as a method of identifying the bacilli of tuberculosis in the urine. They found that in examining any specimen of urine for the bacilli by centrifugalizing methods, the best results were obtained when the specimen was centrifugalized for a period of not less than fifteen minutes at a speed of approximately 2,300 revolutions a minute. Longer than fifteen minutes is apparently unnecessary.

Pus is important, as a centrifugalizing force, in carrying down the bacilli. According to certain established methods, part of the pus should be removed in order to produce better smears; then the pus removed should be examined for bacilli as well as the final sediment. Coincident centrifugalization of part of the unknown specimen to which bacilli from a stock suspension have been added and subsequent coincident staining of both smears on the same slide are advisable.

Simple centrifugalization as a means of finding the bacilli of tuberculosis in the urine is equal to any established method and better than most of them. It would, therefore, seem to be the most satisfactory method for the urologist who does his own laboratory work or who has it done under his own supervision.

Lower<sup>58</sup> favors the use of the anoci-association method of anesthesia from the standpoint of minimizing traumatic and psychic shock. The lipoid solvent anesthetics, such as ether and chloroform, have a special deleterious effect on the kidneys. Albuminuria follows their usage in about a fourth of the cases. In patients with diseased kidneys, the effect of inhalation anesthesia of this type may be enough to produce fatal urinary suppression or persistent albuminuria. Lower thus believes that the use of ether and chloroform is contraindicated in renal operations or when the urinary tract is already carrying an extra load.

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57. Jeck, H. S., and Munch, Margaret A.: Studies in Centrifugalization as a Means of Identifying Tubercle Bacilli in the Urine, *J. Urol.* 18:607, 1927.

58. Lower, W. E.: Anesthesia in Genito-Urinary Operations, *Ann. Surg.* 86: 268, 1927.

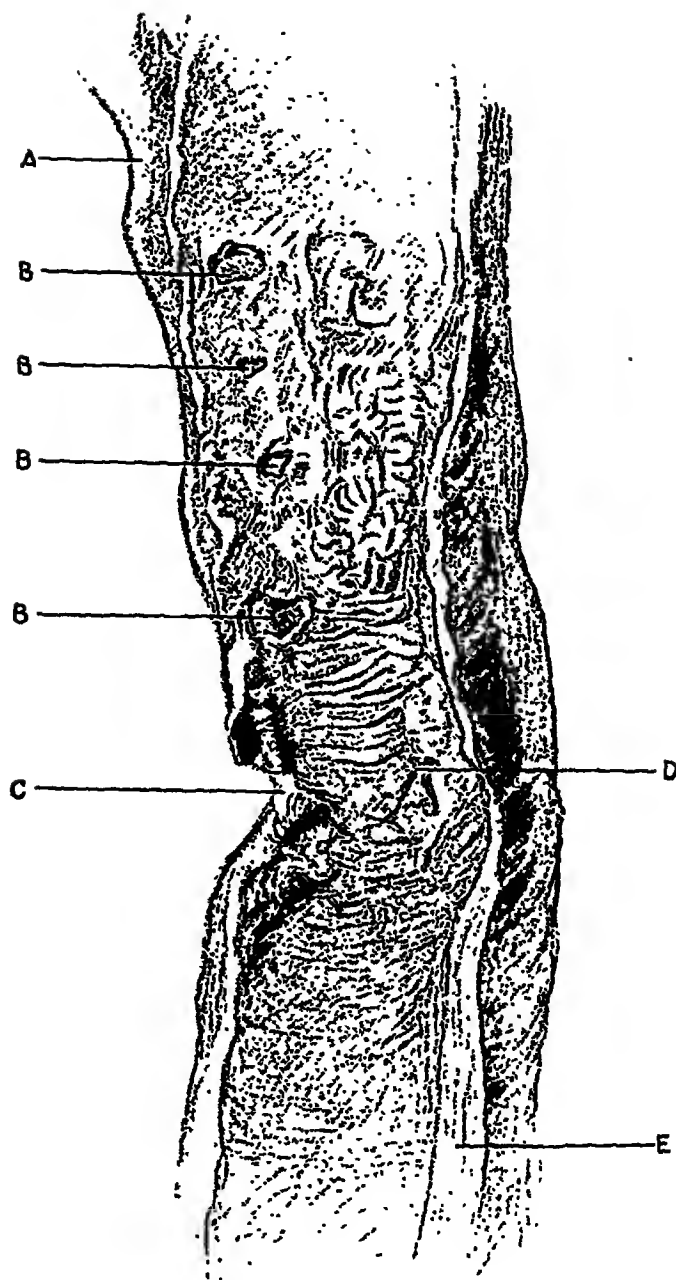


Fig. 1.—Postmortem specimen. *A* indicates the jejunum, adherent to surface of bowel; *B*, four smaller ulcers; *C*, the perforated ulcer; *D*, the narrowing and constriction of lumen, and *E*, marked hypertrophy of wall of colon proximal to ulceration and narrowing of lumen.

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## SIMPLE, NONSPECIFIC ULCER OF THE COLON \*

MAURICE E. BARRON, M.D.

BOSTON

Simple, nonspecific ulcer is a pathologic lesion which occurs in the colon. It may exist as a single lesion or it may be multiple. The fact that it does occur and usually tends to perforate should make one ever mindful of its occurrence.

By simple ulcer is meant an ulcerating lesion which is not due to the action of any specific organism such as the specific ulcer of tuberculosis, syphilis, ulcerative colitis, dysentery, typhoid fever or to the local action of any chemical agent, and which is not secondary or above a malignant tumor causing constriction.

This series comprises fifty-three cases; fifty were collected from the literature and three are cases that I observed. In this series, the cases include simple ulcers of the colon regardless of their location. Both perforated ulcers and chronic latent ulcers have been considered, since in certain patients the ulcers may have been multiple, one ulcer having perforated and the others remaining quiescent. I have included also simple ulcer of the rectum as I believe the etiology and pathology of this disease to be the same as that of simple ulcer on any segment of the colon. I have also included those simple ulcers which, in the process of healing, have caused a stenosing cicatrix, and thus given rise to partial or complete obstruction. In other words, all ulcers of the colon of a nonspecific nature that were studied by autopsy, resection or visualization at time of operation were included.

### HISTORICAL

There is nothing in the American literature regarding this lesion aside from a case report by Lyle,<sup>1</sup> in 1912, and a report of three cases by Dickinson,<sup>2</sup> in 1922, entitled, "Perforating Ulcers of the Cecum." Most of the cases reported are found in the French and German literature.

This disease is not new, and was first described by Cruveilhier<sup>3</sup> in 1830. Since then, there have been many cases reported. No attempt

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\* From Surgical Department of Beth Israel Hospital, Boston, Mass.

1. Lyle, H. H. M.: Simple Ulcer of the Colon: Perforation, *Ann. Surg.* 56:473, 1912.

2. Dickinson, G. K.: Perforating Ulcers of the Cecum, *J. A. M. A.* 78:1792 (June 10) 1922.

3. Cruveilhier, J.: Rectum, *Atlas d'anatomie et pathologie*, 1830-1832, p. 4.

TABLE 1.—*Résumé of Cases Reported Since 1837*

Author	Sex	Age	Preoperative Diagnosis	Location	Perforation	Result
1. Marchesseaux: Bull. Soc. anat. de Paris 12:343, 1837	F	45	Intestinal perforation or peritonitis	Rectum	Perforation	Autopsy
2. Rogee: Bull. Soc. anat. de Paris 13:181, 1838	F	61	No diagnosis	Rectum	Perforation	Autopsy
3. Greenhow: Path. Soc. Newcastle & Colestead, Dec., 1848	M	72	No diagnosis	Splenic flexure	Perforation	Autopsy
4. Lebert: Traité d'anatomie et pathologie, générale et spéciale, 1861, vol. 2, p. 206	M	47	No diagnosis	Splenic flexure	Perforation	Autopsy
5. Idem .....	M	47	Intestinal obstruction	Sigmoid	No perforation	Autopsy
6. Dujardine: Soc. de sc. méd. et Naturelle de Bruxelles, 1864	M	No age	Tumor of spleen, colitis	Splenic flexure	Perforation	Autopsy
7. Claus: Inaug. Diss., Zurich, 1856	M	47	Peritonitis	Splenic flexure	Perforation	Autopsy
8. Dickinson: Tr. Path. Soc. London 18:101, 1867	F	42	Peritonitis	Sigmoid	Perforation	Autopsy
9. Idem .....	M	42	Renal disease	Descending colon	Perforation	Autopsy
10. Robin: Thèse, Paris, 1869	M	66	No diagnosis	Descending colon	No perforation	Autopsy
11. Costin: Brit. M. J. 2:247, 1870	M	45	No diagnosis	Ascending colon	Perforation	Autopsy
12. Lepine: Bull. Soc. anat. de Paris 45:27, 1870	F	70	No diagnosis	Splenic flexure	No perforation	Autopsy
13. Chouppe: Bull. Soc. anat. de Paris 45:322, 1870	M	32	No diagnosis	Hepatic flexure	Perforation	Autopsy
14. Demange: Rev. méd. de l'est, Aug., 1897, p. 500	M	72	No diagnosis	Sigmoid	Perforation	Autopsy
15. Mickle: Brit. M. J. 1:637, 1883	M	45	Peritonitis and perforation	Sigmoid	Perforation	Autopsy
16. Bradbury: Lancet 2:637, 1884	M	30	No diagnosis	Cecum	No perforation	Autopsy
17. Oliver: Lancet 1:424, 1885	No age or sex	No diagnosis	Ascending colon	Perforation	Autopsy	
18. Parker: St. Barth. Hosp. Rep. 23:213, 1887	F	18	Perityphilitis	Ascending colon	Perforation	Autopsy
19. Idem .....	F	49	No diagnosis	Ascending colon and cecum	Perforation	Autopsy
20. Ollier: Loire méd. 11:3, 1892	M	56	Peritonitis	Cecum	Perforation	Autopsy
21. Morel and Scheyron: Soc. de méd. de Toulouse, 1895	M	46	Cancer of cecum	Cecum	No perforation	Examination resected tissue, cured
22. Southam: Brit. M. J. 1:254, 1895	M	67	No diagnosis	Cecum	Perforation	Autopsy
23. Guinard: Thesis, Paris, 1896, no. 324	M	27	No diagnosis	Hepatic flexure	Perforation	Autopsy
24. Morel and Rispaill: Soc. de méd. de Toulouse, 1896	M	67	Intestinal obstruction	Sigmoid	Perforation	Autopsy
25. Gamgee: Brit. M. J. 1:950, 1898	M	28	No diagnosis	Sigmoid	Perforation	No autopsy or pathologic examination, cured
26. Quenu and Duval: Rev. de chir. 26:602, 792, 1902	F	50	Ulcer of rectum	Rectum	No perforation	No autopsy, cured
27. Tedenat, quoted by Quenu and Duval	M	40	Paracecal abscess	Ascending colon	Perforation	No autopsy, cured
28. Idem .....	M	52	No diagnosis	Cecum	Perforation	Incomplete autopsy
29. Idem .....	M	68	No diagnosis	Ascending colon	Perforation	No autopsy, cured
30. Ziekler: Beitr. z. klin. Chir. 67:189, 1910	F	25	Appendicitis	Ascending colon	Perforation	No autopsy, cured

was made to collect a group of these cases for study until 1902. At that time, Quenu and Duval<sup>4</sup> reviewed twenty-seven cases of simple ulcer of the colon reported in the literature, including their own case which presented an ulcer of the rectum. Twenty-five of these patients were studied both in life and at postmortem examinations. Autopsy was incomplete in one case and in another case a histologic and gross study of the resected lesion was made.

In 1920, R. Soupault<sup>5</sup> reviewed twenty-seven cases of perforated ulcers of the colon. In his series, he eliminated ulcers of the rectum, ulcers situated above a stricture, ulcers causing stricture, though the strictures be due to a healed ulcer, and latent ulcers that have not perforated. Since then there have been several cases reported both in the French and German literature.

A brief historical résumé of the cases reported since 1837 is given in the following table.

#### REPORT OF AUTHOR'S CASES

**CASE 1.—History.**—Mr. S. B., a carpenter, aged 55, entered the surgical service of the Beth Israel Hospital on Nov. 4, 1926, with a complaint of pain in right lower quadrant. His family and past history were essentially negative. About two months previously, he had had an attack of pain in right lower quadrant which was not sharp or radiating. At that time, it was not severe enough to keep him in bed. The pain lasted one and a half days and was not associated with nausea or vomiting. The day before entrance to the hospital, he had a similar attack, but much more severe. Pain was localized just to the right of McBurney's point, causing him to double up. He was unable to work at this time. At no time previous to this history had he complained or consulted a physician for any abdominal condition. He was markedly constipated, always using cathartics. There never had been any nausea or vomiting. His stools varied in shape, and he described the color as being like that of weak tea. For two years he had had epigastric distress after meals. He weighed 171 pounds (77.6 Kg.). He had never been jaundiced.

**Physical Examination.**—The patient was a well developed and well nourished, middle-aged man, lying in bed with no objective signs of pain. The skin was moist and the face flushed. There was nothing else of note except marked tenderness of the whole right side of the abdomen. The maximum tenderness seemed to be in a line slightly above McBurney's point on the level with the umbilicus. There was a slight spasm in this region. The costovertebral angles were not tender. The abdomen was tympanitic throughout. No definite mass was made out over the tender area. A provisional diagnosis of acute appendicitis was made, and immediate operation was advised. The results of the urinalysis were negative. Examination showed: white blood cells, 12,300; temperature, 100 F.; the pulse rate, 100, and respiration, 22.

**Operation.**—Nov. 4, 1926: A right rectus incision was made under ether anesthesia, and a small amount of free fluid escaped from the peritoneal cavity. A

4. Quenu, E., and Duval, P.: Simple Ulcer of the Large Intestine, *Rev. de chir.* 26:692, 792, 1902.

5. Soupault, R.: Contribution to the Study of the Perforation of Simple Ulcer of the Colon, *Rev. de chir.* 58:480, 1920.



The following report was made at this time from the x-ray department: The tone of the stomach was good, and peristalsis was normal; the outline of the stomach was regular while the duodenum showed constant irregularity. Examination made five hours after the ingestion of the barium meal showed a small residue in the stomach (from 10 to 15 per cent). The head of the meal was in the distal portion of the colon (hypermotility). Examination made twenty-four hours after the barium meal showed the head of the meal in the ampulla of the rectum. The entire colon was empty. Examination of the colon with an opaque enema did not show any obstructive lesions. The cecum and ascending portion of colon showed finger-like defects, but its outline was rather smooth. The terminal ileum was well filled, distended, and also showed irregular filling. The inferior border of the transverse portion of colon was slightly irregular and appeared to be fixed.

The hypermotility of the colon when examined five hours after the barium meal and also the rapid emptying of the colon after the twenty-four hour examination suggested marked colonic irritation. This, together with the filling defect in the terminal ileum, cecum and ascending portion of the colon, definitely pointed to a pathologic process in that region. The entire picture was not characteristic of a malignant condition. There was a possibility of a tuberculous lesion.

The patient did not appear again until his next admission to the hospital on Aug. 15, 1927. This was the first time that he came to my attention. Again, the chief complaint was pain in right side of the abdomen. The patient said that he had been operated on at the Beth Israel Hospital seven months before. He had been discharged as cured, but he had never felt well since his operation. The week before his second admission, the pain was rather severe and stabbing, and seemed to be getting worse. The family physician said that he had felt a tumor in the patient's right side since he left the hospital, and that the tumor was now growing larger. His appetite was good. During the past four days, he had been constipated, requiring enemas. Previous to this, he said that he had had bowel movements about eight times a day; the stools were watery and accompanied by considerable gas. There had not been any nausea or vomiting. His best weight was 210 pounds (95.2 Kg.) one year before admission to the hospital. At the time of the previous operation, he weighed 171 pounds (77.6 Kg.); his present weight was 164 pounds (74.4 Kg.).

On his discharge from the hospital after his previous operation, he gained in weight, but recently he had been losing. His past history and family history were the same as on the previous admission. The physical examination was essentially the same, except for the abdominal examination. There was a scar over the right rectus muscle as a result of the previous operation. His right side was rigid and spastic all over. There was a palpable mass about the size of a small grapefruit which seemed to be somewhere in the center, between the right iliac fossa and the right costal margin. This mass was extremely tender to the touch. The left side of the abdomen was soft and tympanitic throughout and tenderness was not noted. A provisional diagnosis of malignancy of the colon with a secondary inflammation was made. The patient had a slight elevation of temperature; the pulse rate was not increased. An x-ray report two days after admission showed the following: The tone of the stomach was good; peristalsis was normal; the outline was regular, and the duodenum did not show any filling defect but appeared to be fixed. Examination five hours after the ingestion of a barium meal in the stomach showed the head of the meal in the sigmoid flexure. The entire colon was well filled. The cecum was irregular and showed a definite filling defect. Examination twenty-four hours after the barium meal showed

TABLE 1.—Résumé of Cases Reported Since 1837—Continued

Author	Sex	Age	Preoperative Diagnosis	Location	Perforation	Result
31. Lyle: Ann. Surg. 50: 473, 1912	F	20	Appendicitis	Ascending colon	Perforation	No au- topsy, cured
32. Runke: Deutsche Ztschr. f. Chir. 147: 234, 1918	M	53	Strangulated hernia	Hepatic flexure	Perforation	Autopsy,
33. Soupault: Rev. de chir. 58: 480, 1920	F	22	Appendicitis	Ascending colon	Perforation	No au- topsy, cured
34. Bazy: Bull. et mém. Soc. de chir. de Paris 40: 416, 1920	M	63	Obstruction, cancer	Ascending colon	Perforation	Autopsy
35. Idem .....	M	20	Appendicitis	Cecum	Perforation	No au- topsy, cured
36. Gregoire: Bull. et mém. Soc. de chir. de Paris 40: 420, 1920	M	55	Appendicitis	Sigmoid	Perforation	No au- topsy, death
37. Sleur: Bull. et mém. Soc. de chir. de Paris 40: 421, 1920	M	30	No diagnosis	Cecum	Perforation	Autopsy
38. Lardennois: Bull. et mém. Soc. de chir. de Paris 40: 447, 1920	M	52	Peritonitis	Cecum	Perforation	Autopsy
39. Schoemaker, quoted by Soupault	M	No age	Peritonitis	Sigmoid	Perforation	Autopsy
40. Levy: Deutsche Ztschr. f. Chir. 165: 366, 1921	M	No age	Appendicitis	Cecum	No perfora- tion	No au- topsy, cured
41. Ecot and Richard: Bull. et mém. Soc. anat. de Paris 112: 138, 1922	No age or sex		Obstruction	Ascending colon	Perforation	No au- topsy, cured
42. Dickinson: J. A. M. A. 78: 1792 (June 10) 1922	M	No age	Appendicitis	Cecum	Perforation	Autopsy
43. Idem .....	M	22	Chronic appen- dicitis, chronic cholecystitis	Cecum	Perforation	Autopsy
44. Idem .....	M	56	Appendicitis	Cecum	Perforation	No au- topsy, cured
45. Bowen: Guy's Hosp. Rep. 72: 441, 1922	F	No age	Intestinal perforation	Sigmoid	Perforation	No au- topsy, death
46. Idem .....	F	27	No diagnosis	Cecum	Perforation	No au- topsy, does not state
47. Challer and Mallet-Guy: Arch. d. mal de l'app. digestif. 13: 521, 1923	M	50	Tuberculous peritonitis, tuberculous enteritis	Ascending colon	No perfora- tion	Autopsy
48. Mintz: Zentralbl. f. Chir. 50: 1208, 1923	F	18	Intussuscep- tion	Cecum	No perfora- tion	Resection, pathologic examination, cured
49. Broere: Nedrl. Tijdschr. v. Geneesk. 67: 2274, 1923	F	80	No diagnosis	Sigmoid	Perforation	Autopsy
50. Boss: Beitr. z. klin. chir. 140: 40, 1927	M	38	No diagnosis	Sigmoid	Perforation	No au- topsy, cured
51. Barron: In the text.....	M	56	Appendicitis, malignancy	Ascending colon	Perforation	Autopsy
52. Barron: In the text.....	F	23	Appendicitis	Cecum	No perfora- tion	No au- topsy, cured
53. Barron: In the text.....	F	32	Simple ulcer of rectum	Rectum	No perfora- tion	No au- topsy, cured

large, inflammatory mass was found at the hepatic flexure, firmly tied down to all the adjacent structures. The mass was covered by omentum. The distal portion of the ascending colon seemed to be adherent to the transverse colon. The adhesions were separated without much difficulty, and a small opening was found in this inflammatory mass from which thick, greenish pus escaped. The appendix was retrocecal and did not show evidence of acute inflammation. It was removed in the usual manner. The abdomen was closed in layers with two cigaret wicks.

The patient made an uneventful convalescence. There was a purulent discharge from the abdominal sinus which eventually cleared up, and the patient was discharged well, eighteen days after operation. The wound was well healed throughout. The patient was advised to come back for further x-ray study, but he did not return to the hospital until Dec. 14, 1926.

3 cm. thick, representing a fecal fistula. The mucosa was thick, almost gangrenous about the opening.

On the ascending colon, distal to the perforation and under the site of the pocket was a shallow ulcer 1.5 by 1 cm. The base of this ulcer rested on surrounding fatty and scar tissue. Four other smaller ulcers were present, 1 cm.,



Fig. 2 (case 1).—A indicates the perforation on the ascending colon; the barium can be seen escaping in a small amount. The roentgenogram was taken following a barium enema.

4 cm. and 1 cm. in diameter, occurring at intervals of about 1.5 cm. The ulcers were pale, the edges flush with the surrounding mucosa. No communication could be found between the base of the ulcer and the surrounding scar tissue.

Microscopic examination of the ulcers showed the base made up of fibroblastic tissue which extended almost to the surface. The amount of granulation tissue was

that the entire colon was practically empty, except for a small amount of barium in the distal portion of the colon. The region of the gallbladder did not show any evidence of stones.

The nonfilling, the irregularity and the hypermotility of the colon suggested a lesion in the cecum, which I believed would be revealed after x-ray examination made after a barium enema.

The patient's temperature gradually rose and the pulse rate increased. Pain was becoming worse and the mass was growing larger. Operation was advised on August 25, ten days after admission. The results of the urinalysis were negative, and the white blood count was 13,150. The Wassermann reaction of the blood was negative.

*Operation*—August 25: A right rectus incision, 4 inches (10.16 cm.) long, was made over the mass under ether anesthesia. On opening the peritoneal cavity, a large amount of a thick, greenish-yellow, foul smelling, pus escaped. Exploration revealed a large abscess cavity between the ascending colon and the lateral abdominal wall. There were many pockets which were freed so that one large abscess cavity resulted. The wound was closed in layers with two cigaret wicks and one rubber tube drain. On account of the severe inflammatory reaction and the large amount of pus in the abscess cavity, nothing further was done. Swabs from the abscess at the time of operation showed colon bacilli and a few short chained streptococcus.

The patient made an uneventful convalescence from the immediate effects of the operation. A considerable amount of pus drained until the sixth day when he developed a fecal fistula. On September 8, his head blocks were removed and he was taken off the Fowler's position; the temperature and pulse were normal. Fecal matter was still draining. On September 12, there was a marked inflammatory reaction around the edges of the wound. The temperature and pulse rate were normal. On September 20, the wound stopped draining. There was a sudden rise in temperature and pain was felt in the right side. Flaxseed poultices were applied and the wound began to drain again, but from that time on the patient became progressively worse and died on October 14, seven weeks after operation.

*Postmortem Examination*.—A large abscess was found in the right upper quadrant of the abdomen. The lowest portion of the right lobe of the liver formed the roof of the abscess cavity; the hepatic flexure, the medial wall, and the abdominal wall, the lateral wall. That portion of the liver which formed the roof of the abscess was gangrenous and necrotic. On the ascending colon near the hepatic flexure, there was a large perforation.

*Pathologic Report*.—Oct. 14, 1927: The specimen consisted of 5.5 cm. of terminal ileum, cecum, ascending colon with a portion of transverse colon, the whole measuring 30 cm. in length. The external surface of the cecum and the ascending colon was covered by a mass of densely adherent mesentery and scar tissue. At the hepatic flexure, this mass of adhesions was separated to form the wall of a pocket, roughly 7 cm. in diameter. A loop of jejunum was bound to the outer surface of the pocket by dense scar tissue. The wall of the pocket was made up of fibrous tissue 3 mm. thick, lined by a greenish, necrotic membrane. Beyond the pocket, the scar tissue stopped abruptly. A portion of omentum was adherent to the transverse colon. The adhesions were readily broken.

When the intestine was laid open, nothing remarkable was found in the ileum and jejunum. The cecum was lined by a reddish thickened mucosa. The wall of the ascending colon was thickened and fibrous and showed an irregular opening

*Pathologic Report.*—A small piece of omental tissue the size of a lima bean was examined. Gross examination showed that it was hemorrhagic, fat tissue. The tube was congested, thickened and showed fibrous adhesions. The cyst was the size of an orange, containing clear contents. The vermiform appendix, 6 cm.

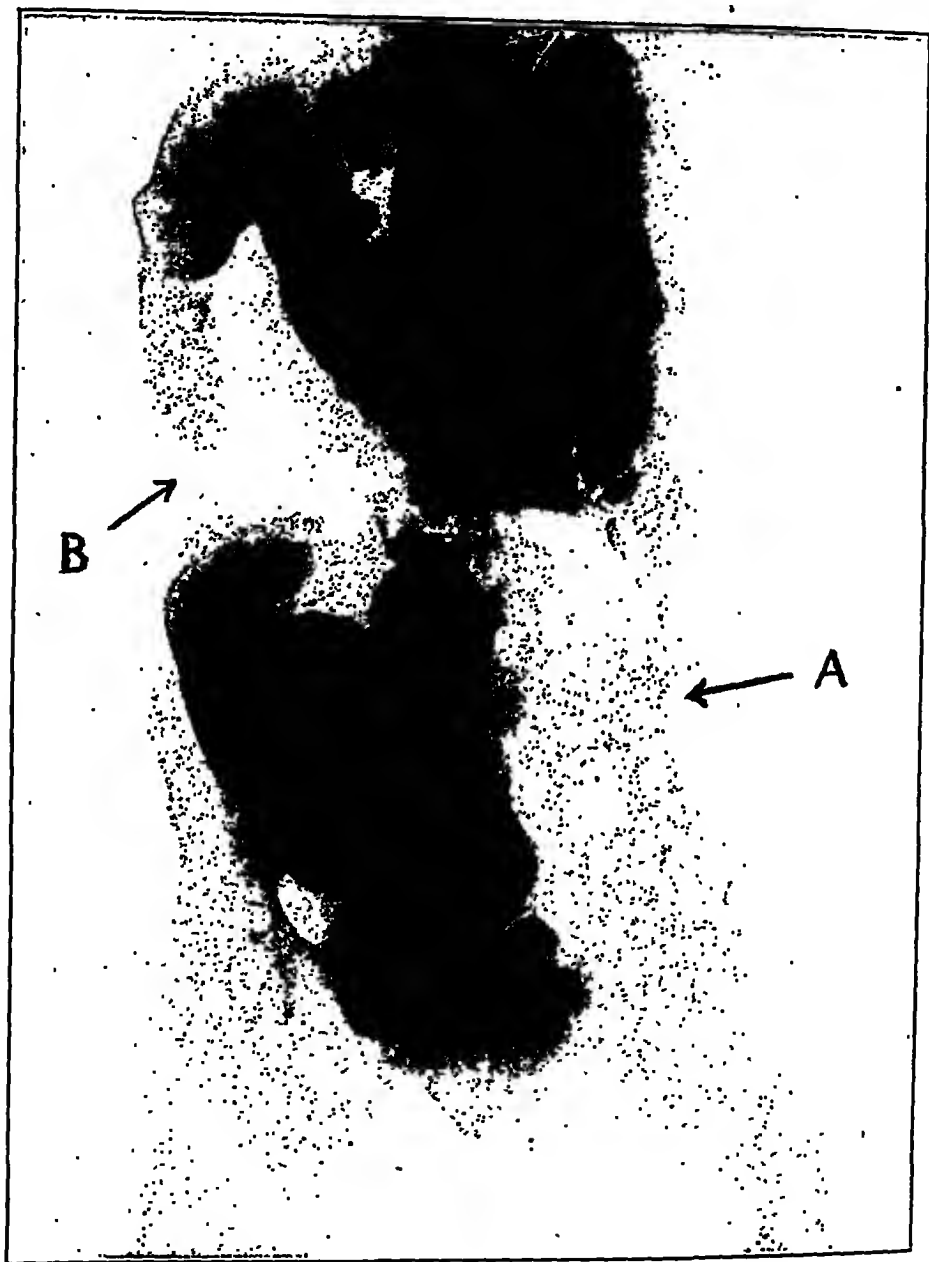


Fig. 3 (case 2).—*A* indicates the cecum, showing the filling defect three weeks after operation. *B* shows the spasm of the descending colon opposite the site of the lesion. This observation has been stressed by Carmen and others. (Roentgen-ray examination five years later showed a normal cecum.)

in length, did not show any acute signs of inflammation. Microscopic examination of omentum revealed some hemorrhage into the adipose tissue, with a marked polymorphonuclear leukocyte infiltration.

small. A cellular exudate of lymphoid, plasma and polymorphonuclear cells, relatively small in amount, was present. The surface was covered by detritus. There was a marked increase in connective tissue beneath the ulcer, associated with atrophy and disappearance of muscle fibers and extending into surrounding fatty tissue. Large collections of lymphoid and plasma cells were present and a few polymorphonuclears.

Following the patient's death, the x-ray films were again studied. From the last x-ray examination, it now seemed rather evident that there was a small perforation in the distal portion of the ascending colon through which a small amount of barium could be seen escaping from the lumen of the bowel. This was overlooked prior to the operation. However, had this complication been noted, I hardly think that anything else could have been done for this man in the presence of the severe inflammatory reaction and the collection of pus in the abscess cavity. It seemed to me that proper drainage of the abscess was sufficient treatment. The fact that the fecal fistula was established and that the temperature returned to normal, would seem as though the abscess cavity had been properly drained and that there were no fecal contents remaining within the abdominal cavity. It is possible that there was another abscess which did not drain sufficiently and which caused necrosis of the liver, which ultimately resulted in the patient's death.

**CASE 2.—History.**—Miss M. G., aged 23, entered the surgical service of the Beth Israel Hospital on Feb. 23, 1923, with a complaint of severe pain in right lower quadrant. The onset of the condition began two days previously. At first, pain was generalized, then it seemed to localize itself in right lower quadrant. She vomited several times during the day of entrance. There had never been any abdominal pain previously. There was no blood in the vomitus, and the patient had never noticed any blood in the stools. Cough or hemoptysis was not noted. The menstrual history and the results of the urinalysis were negative. The leukocytosis was 13,000. The family history and past history were negative.

**Physical Examination.**—The patient was a well developed and well nourished young woman, lying in bed complaining of severe pain in right lower quadrant. The temperature was 99 F., the pulse rate, 90. There was nothing else of note except for the abdominal examination which revealed marked tenderness in the right lower quadrant with spasm of the muscles over this region. A definite tumor or mass could not be felt. Maximum tenderness was elicited over McBurney's point. Other than this, the abdomen was soft and tympanitic. A provisional diagnosis of acute appendicitis was made, and immediate operation was advised.

**Operation.**—The operation was performed under ether anesthesia on the night of entrance to the hospital. A right rectus incision was made. The appendix appeared normal. On the anterior lateral surface of the cecum, there could be seen and felt an indurated, inflamed, hard mass over which some omentum adhered. The omentum was separated from the cecum, and a piece covering this mass was excised, revealing what apparently was the base of an ulcer about the size of a quarter. There was no evidence of perforation. The ulcer was round and hard, resembling a callous peptic ulcer. Three mattress sutures of silk were placed through the serosa about the ulcer and it was covered with omentum. There was no evidence of tuberculosis as far as could be seen. A simple cyst of the right ovary about the size of an orange, together with the right tube, was also excised. The abdomen was then closed in layers in the usual manner. The patient made an uneventful convalescence and was discharged well in fourteen days.

half dollar on the right lateral and posterior wall of the rectum about 6 inches from the anus. In the center of the ulcer a bleeding point could be seen from which this profuse hemorrhage apparently came. The ulcer was packed with iodoform gauze, and the patient returned to bed in good condition. On April 9, the iodoform gauze was removed from the rectum. The patient never showed any signs of bleeding from the rectum since and was discharged well on June 12.

The results of the examination of the stool were negative. The patient was kept in the hospital until this time on account of the acute arthritis of the right ankle, which eventually disappeared. The results of the urinalysis were always negative. On May 25, the white blood count was 8,600; the red blood count, 4,252,000; polymorphonuclear neutrophils, 68 per cent, lymphocytes, 22 per cent, and large mononuclears, 9 per cent.

On March 28, 1928, the patient reported by letter that she had never had any diarrhea or bleeding from the rectum since she left the hospital. She has enjoyed perfect health and has since given birth to another child.

On April 16, 1928, at my request, the patient returned for a roentgen-ray examination of the colon. The following report was made: "The roentgen examination of Mrs. S. B., was made on April 16, 1928. Part examined: Colon

TABLE 2.—*Age and Sex Incidence*

Ages	Number of Females	Number of Males
15-20.....	2	None
20-30.....	4	4
30-40.....	None	4
40-50.....	8	8
50-60.....	1	7
60-70.....	1	5
70-80.....	2	2
No age specified, 5; no age or sex specified, 2		

(enema). The observations are as follows: The examination with an opaque enema shows the entire colon well filled and regular in contour with normal haustration throughout. No abnormalities could be noted."

#### AGE AND SEX

In this series of fifty-three cases, there were thirty-four males and seventeen females; in two cases the sex was not specified. One is immediately impressed with the fact that there are twice as many males as females. Apparently this seems to be a disease in which the male is more prone to be stricken than the female. The same observation has been made by many investigators regarding peptic ulcer.

The youngest female was 18 years of age, and the oldest 80; the youngest male was 20, and the oldest, 72. The average age for the group was 41.25 per cent years; for males, it was 43.5 per cent years, and for females, 41.06 per cent years, making the average age of both sexes about the same. Among the males, there was no age specified in three cases, and among the females, no age specified in two cases. Among the males, the greatest incidence occurred between the ages of 40 and 50; then 50 and 60, and then 60 and 70. Among the females,

*X-Ray Examination.*—X-ray examination made three days before the patient was discharged from the hospital showed that the stomach was orthotonic with normal peristalsis; the outlines of the greater and lesser curvatures were regular; the duodenum was displaced toward the lesser curvature. Examination made three hours after a barium meal showed the head of the meal in the small bowel. The stomach was empty. Examination made six hours after the meal showed the head of the meal in the terminal ileum. This marked delay of barium entering the cecum was probably due to adhesions. Twenty-four hours after a barium meal, examination showed the height of the meal in the ampulla. The cecum and the ascending colon still contained barium. A barium enema was given. The cecum was irregularly filled. The condition at the ileocecal region was pathologic and was probably due to adhesions.

At my request, the patient returned almost five years after the operation for reexamination. She said that she was feeling well since operation. She did not feel any pain. Her appetite was good and bowel movements occurred daily without the aid of cathartics. The report of the x-ray examination was as follows: "The roentgen examination of Miss M. G., was made on December 10, 1927. Part radiographed:—Colon. The findings are as follows:—The examination of the colon with opaque enema shows the entire colon well filled, regular in contour, but rather atonic. The cecum is well filled. No abnormalities could be noted."

*CASE 3.—History.*—Mrs. S. B., aged 32, married, entered the surgical service of the Beth Israel Hospital on March 26, 1922, complaining of bleeding from the rectum. Seven weeks before entrance, she noticed the bleeding after a bowel movement. The stool was rather large and bright red. There was a slight pain in the left lower quadrant which came on just before defecation. This pain radiated downward to the anal orifice. Since then, there had been three attacks similar to the previous one, with a considerable loss of blood each time. Diarrhea did not occur at any time, nor was there any mucus in the stools. The patient was rather constipated. Her appetite was good and she was not troubled with nausea or vomiting. Dysuria or hematuria were not noted. The family history was unimportant. The past history showed that she had had gonorrhea four years ago, but had not had any operations. Her husband was living and well; there was one child, also living and well. There had not been any miscarriages.

*Physical Examination.*—The patient was a well developed and well nourished young woman, lying in bed complaining of general weakness and pain in left lower quadrant. The skin was clear and of good color. There was nothing else of note except for the abdominal examination which revealed a soft and tympanitic region, although no mass or organs were felt. There was slight tenderness and resistance in the left lower quadrant.

*Course.*—On March 28, the patient had two loose, bloody stools. Considerable pain was felt in the left lower quadrant. On April 3, she developed an acute arthritis of the right ankle. On April 6, she had a profuse hemorrhage from the rectum. She immediately went into collapse and became extremely pale; the mucous membranes were blanched, and she complained of air hunger. The pulse rate was 150 and barely perceptible. The blood pressure had fallen to 60 systolic, 35 diastolic. A blood transfusion of 750 cc. of blood was given. Following the transfusion, the pulse rate came down to 120 and the blood pressure rose to 90 systolic and 60 diastolic. Three hours after the transfusion, the pulse rate was still 120; the blood pressure had increased to 100 systolic and 50 diastolic.

On April 7, the patient was still bleeding from the rectum in small amounts. Sigmoidoscopy revealed a large, round, circumscribed ulcer about the size of a



Cruviellhier,<sup>3</sup> in his "Atlas of Pathologic Anatomy," expresses the opinion that the extremity of the intestine may be the seat of a simple ulcer similar to that of the stomach and duodenum.

It would seem that simple ulcer of the colon must be a manifestation of the same general disease as peptic ulcer, if there is a common etiologic factor in the production of these lesions on the various segments of the gastro-intestinal tract. This fact is particularly impressive since ulcer of the intestine is found not infrequently in association with ulcer of the stomach.

It is not unusual to find multiple ulcers of the duodenum and stomach in the same patient; there are numerous cases recorded that prove this. Recently Pickhardt<sup>10</sup> reported a case in which there were several ulcers in the stomach and duodenum, two of which, one in the stomach and one in the duodenum, had perforated. The fact that one is ready to accept the etiology as being the same when the lesion occurs both in the stomach and duodenum, is sufficient reason to accept the same etiologic factor, even though the lesion is farther down the intestinal tract. If one may correlate ulcer of the stomach with ulcer on any other part of the intestinal tract as having a common etiology, it is obvious that there may be a healed ulcer of the stomach and an active ulcer on the colon, or, from the same cause, a simple ulcer of the colon may exist alone. If ulcer of the colon and peptic ulcer are to be considered as having common etiology, the various theories that have been advanced for peptic ulcer must be taken up.

The theories that have been advanced regarding the initial cause of peptic ulcer may be classified according to whether or not the initial lesion is regarded as inflammatory, neurogenic, circulatory, bacterial, toxic, digestive or mechanical. The symptoms and the pathologic histology would seem to indicate that practically all of these theories might apply to ulcer of the colon. There are certain theories, however, that seem to explain the etiology more than the others.

The outstanding symptom seems to be constipation, of which there are twenty-one cases; constipation was not present in five cases, and in twenty-seven cases, it was not recorded. One must take into consideration that some of the early case reports were rather incomplete, and it is possible that in the twenty-seven cases in which constipation was not mentioned that there might have been many in which constipation was present. What rôle then can constipation play in the etiology of this condition? This would necessarily bring it under the head of the mechanical theory, either direct or indirect. This view is held by many observers (Quenu and Duval,<sup>4</sup> Soupault,<sup>5</sup> Delafield and Prudden<sup>11</sup>). Under this

10. Pickhardt, O. C.: *Ann. Surg.* 87:143, 1928.

11. Delafield and Prudden: *Textbook of Pathology*, ed. 12. New York, William Wood & Company, 1923, p. 775.

the greatest number occurred between the ages of 20 and 30, then between 40 and 50. It would seem from this study, that the average age is the same for males and females and that it is not essentially a disease of the old.

#### ETIOLOGY AND PATHOGENESIS

Many observers are of the opinion that simple ulcers may occur in any part of the gastro-intestinal tract, and aside from ulcers of the stomach and duodenum, there are many cases reported of ulcers of the esophagus, the jejunum, the ileum and of the various segments of the colon. Bolton,<sup>6</sup> in his book on "Ulcer of the Stomach," said:

It is not uncommon to find ulcers in other portions of the alimentary canal in association with gastric ulcer. Such an association is commoner in the case of ulcers of obviously infective origin, but also sometimes occurs in the simple, acute gastric ulcer. Such acute ulcers are found in the duodenum, esophagus, lower end of ileum and the colon.

In his series of twenty-four cases of ulcer of the stomach, additional ulcers in the same patient were found as follows: in the duodenum and stomach, fifteen cases; in the esophagus and stomach, four cases; in the ileum and stomach, three cases; in the stomach, two cases. In the present series which was studied, there was found four cases of ulcer of the colon in association with ulcer of the stomach (cases 4, 7, 46 and a case reported by Chrostek quoted by Quenu and Duval<sup>4</sup>), and two cases of ulcer of the colon in association with ulcer of the ileum (cases 2 and 12). Combes<sup>7</sup> has collected a series of thirty-six cases of simple ulcer occurring on the small and large bowel, divided as follows: seven in the jejunum, twelve in the ileum, five in the cecum, six in the colon, three in the sigmoid and three in the rectum. Gandy<sup>8</sup> studied a series of fifteen cases, divided as follows: end of the duodenum, one; jejunum, two; ileum, seven; cecum, two; hepatic flexure, one, and sigmoid, two. Vidal,<sup>9</sup> writing on "Ulcers of the Rectum," states: "Simple ulcers may be found throughout the whole length of the large intestine and even in the small intestine and that he has seen a few cases of chronic ulcers of the rectum." When the ulcer was single, he has only found it posteriorly. One of his patients, a man, aged 40, had symptoms of a simple ulcer of the stomach, and he believed that the ulcer of the rectum was of the same nature.

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6. Bolton, C.: *Ulcer of the Stomach*. London, Edward Arnold, 1913, p. 35-35.

7. Combes, C.: *Simple Ulcer of the Intestine*, Thesis. Toulouse, 1897.

8. Gandy, C.: *Hemorrhagic Necrosis of Toxemia and Simple Ulcer*, Thesis. Paris, 1899.

9. Vidal, E.: Rectum in "Dictionnaire encyclopedique des sciences medicales." 1874-1881, vol. 2, pp. 678-690.

the feces may pass into the peritoneal cavity; or the perforations may be partly closed by adhesions, and abscesses or sinuses into the surrounding soft parts may be formed.

The question arises as to whether a catarrhal inflammation of the cecum or colon is primary, and ulceration a secondary manifestation. A controversy has existed for many years in regard to chronic gastritis associated with gastric ulcer. It has been held by some authors that ulcer was secondary to a chronic gastritis. I feel that it is the popular belief that a chronic gastritis is associated with, and probably secondary to, the ulcer. It would seem logical that the same condition exists in the cecum or in other parts of the colon. An ulcer being present, it may follow that secondary inflammation, either of a mild or severe character, may ensue.

According to Kocher,<sup>15</sup> the distention as a result of constipation, obstruction or impaction of feces produces a venous stasis at first in the corresponding segment of the mesenteric artery; ecchymosis follows, then there is a desquamation of the poorly nourished epithelium, and a superficial necrosis of the mucosa is produced. As a result of the experiments of von Greyerz and von Schimodeira,<sup>16</sup> there is a diminution in the arterial blood flow soon after distention occurs. The intestine becomes pale, and ulcers may appear even at this stage. After the distention is released, the intestine becomes deep red; a sign of venous stasis. As experimental ulcers occur as early as four or five days following distention with air, they feel that through venous stasis as a result of distention, nutritional disturbances occur in the intestinal wall, producing ulcers. Kocher and Prutz<sup>17</sup> consider venous stasis and its resulting thrombus formation the essential cause for the formation of these ulcers. According to Rosenheim,<sup>18</sup> the successive stages of ulceration are produced as follows: Intestinal stasis, progressive accumulation and more or less hardening of the contents, then fermentation; constant increase in the number and virulence of the bacteria, chronic inflammatory process, disorders of nutrition and ulcerating lesions. These are the theories of constipation as a mechanical factor: erosion by direct trauma, such as fecaloma, fruit seeds, etc., on the one hand, and the other, distention, due to overloading of the bowel, atony, or obstruction due to impacted feces.

The mechanical theory alone hardly seems to explain the etiology of this lesion, with constipation so universal and widespread. It would seem as though ulcer would be a much more common condition. It cer-

15. Kocher: *Deutsche Ztschr. f. Chir.*, 1877, vol. 5.

16. Von Greyerz and von Schimodeira: *Beitr. z. Chir.* 22:229. 1911.

17. Kocher and Prutz: *Arch. f. klin. Chir.*, 1900, vol. 60.

18. Rosenheim: *Ztschr. f. klin. Med.* 54:475, 1904.

theory, there could be produced the so-called stercoral or decubitus ulcer (case 49). "This type ulcer results in cases of obstipation from a crack or fissure in the mucosa which becomes infected and by extension develops into an ulceration" (Rankin<sup>12</sup>). According to Lyon and Bartle,<sup>13</sup> stercoral or decubital ulcers are mostly confined to elderly persons, and frequently to bedridden patients. "Through lack of the proper nourishment of the body, the coils of the intestines are not changed in their position sufficiently to aid the weakened bowel musculature to pass on its contents completely enough and stagnation occurs. Hardened masses of feces form in the colon and become agglutinated to the mucosa and when they are eventually pushed along through purging, or what not, ulceration quickly follows through secondary infection, attacking the denuded bowel wall. Perforation may take place."<sup>13</sup> This may explain certain ulcers in the rectum or in the sigmoid where the fecal mass may become exceedingly hard, but this can hardly be true in the cecum and ascending colon where the contents are normally fluid, and the patients in this series were not really old, with the possible exception of case 49.

Erosions, fissures and cracks might be caused by foreign bodies such as fruit pits and seeds (case 1). In this case, there was an obstruction due to an ulcer and the foreign bodies may have been lodged at the constriction later, making the occlusion complete.

Stengel and Fox<sup>14</sup> describe ulceration of the cecum in the following manner: "Typhilitis or cecitis may be due to irritation of the intestinal contents in consequence of constipation (stercoral typhilitis)." Typhilitis is probably generally of the simple catarrhal variety, but in obstinate constipation or obstruction of the colon, ulceration may occur. Perforations or extension to the surrounding tissues is the rarest of all consequences. Usually the latter is secondary to the inflammation of the vermiform appendix. Catarrhal inflammation of the cecum, according to Delafield and Prudden,<sup>11</sup> is not uncommon. It is usually produced by an habitual accumulation of feces in this part of the intestine. The course of the inflammation is usually chronic but marked by acute exacerbations. At first, the mucous membrane undergoes ordinary changes of chronic catarrhal inflammation. To this may succeed a slow suppurative inflammation which extends through the wall of the intestine and gives rise to ulcers and perforations. Through these perforations,

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12. Rankin: *Surgery of Colon*, New York, D. Appleton & Company, 1926, p. 104.

13. Lyon and Bartle: *Tice Practice of Medicine*, Hagerstown, Md., W. F. Prior Company, 1924, vol. 7, p. 615.

14. Stengel and Fox: *Textbook of Pathology*, ed. 6, Philadelphia, W. B. Saunders Company, 1915, p. 636.

sclerosis, but no endarteritis. The capillaries were dilated and there was a diffuse hemorrhagic infiltration. Arteriosclerosis can produce infarcts and thrombi, lesions effecting a small portion of the colon or a large segment of the colon by cutting off the blood supply. Quenu and Duval<sup>4</sup> feel that the thrombosing endarteritis existed in the region of the ulcer in case 26. Lyon and Bartle<sup>18</sup> describe a thrombotic and embolic ulceration. They say: "Any part of the gastro-intestinal tract may be involved by this type of lesion, but it is seen more usually in the jejunum, ileum and colon."

Boss<sup>21</sup> holds that ulcers occur, as a rule, not as a primary lesion, but as a secondary manifestation, due to embolism or thrombosis of the arteries of the mesentery.

#### PATHOLOGY

Simple ulcer of the colon may be situated on any segment of the large intestine as shown in table 3.

The lesion may occur as a single ulcer or may be multiple. In thirty-seven cases, the ulcer occurred as a single lesion, and in sixteen cases

TABLE 3.—*Locations of Ulcer of the Colon*

Cecum.....	15	Splenic flexure.....	5
Ascending colon.....	12	Descending colon.....	2
Ascending colon and cecum.....	1	Sigmoid.....	11
Hepatic flexure.....	3	Rectum.....	4
Transverse colon.....	0		

they were multiple. When the ulcers were multiple, they were usually close to each other and there were never more than six. The lesion occurred most often on the cecum. The right half of the large bowel seemed to be a more frequent seat than the left, occurring in the right in thirty-one cases and on the left in twenty-two cases. This seems rather hard to explain since, as I have stated elsewhere, the contents of the cecum are normally fluid.<sup>12</sup> Since there were eleven cases with ulceration, either single or multiple, on the sigmoid, the question naturally arises as to whether these lesions were not diverticulitis or diverticulosis as the latter condition occurs so frequently on this portion of the colon. As these cases were all studied at postmortem examination or at operation, it seems that this question could be well ruled out. In a study of 118 patients who had diverticulitis, Judd and Pollock<sup>22</sup> found that there was no demonstrable narrowing of the lumen of the colon below the site of the diverticula, and furthermore, it is rather unusual to find diverticula in a colon which is markedly obstructed. It is interesting to note

21. Boss, W.: Perforated Ulcer of the Large Intestine, *Beitr. z. klin. Chir.* 140:40, 1927.

22. Judd and Pollock: *Ann. Surg.* 80:425, 1924.

tainly would not be considered that constipation, directly or indirectly, could cause simple ulcer of the small intestine. The same holds true of foreign bodies such as fruit pits, seeds, etc. Frequently, one sees patients who have swallowed foreign bodies which either pass through the gastro-intestinal tract or are removed surgically; the formation of an ulcer, as a result, is rare. It would seem that the foreign bodies are immediately enveloped by the soft fecal mass, and unless the object is a large one, its hard or rough edges seldom come in contact with the wall of the bowel. The theory advanced that venous stasis is a result of distention due to constipation could not explain the etiology in all cases. It does not seem that the etiology of simple ulcer of the colon can be any more explained than the etiology of peptic ulcer, and since I feel that simple ulcer is a manifestation of a general pathologic condition as gastric ulcer is, venous stasis as a result of a general condition such as a toxemia, regardless of its origin, may play an important rôle in the etiology, but not as a result of distention due to constipation.

In an exhaustive study of ulcerations of the gastro-intestinal tract, Gandy<sup>8</sup> came to the conclusion that simple ulcer of any part of the digestive tract is a manifestation of a general toxemia either of infectious or other origin. The toxemia produces an acute hemorrhagic necrosis by way of the blood stream due to hemorrhagic infarct; then follows sloughing, hemorrhagic erosion, ulceration of the mucosa, and finally, a deep ulceration. Rosenow strongly advances the bacterial theory based on the specific affinity of certain organisms for certain parts of the digestive tract. Rosenow, according to Mayo,<sup>19</sup> maintains that certain forms of bacteria injected through the blood stream cause ulcer of the bowel, especially of the cecum. Other forms cause ulceration in the alkaline small intestine or in the acid stomach. Dickinson<sup>2</sup> believes the infection takes place in the adenoid tissue of the cecum first and then extends to the mucosa giving rise to ulceration. Intestinal parasites may be an etiologic factor as described in case 48. Stahr<sup>20</sup> studied several cases in which he felt that the parasites were the causative factors in the production of simple ulcer of both the large and small bowel.

Under the circulatory theory, one must consider diseases of the vessel walls, such as atheroma and endarteritis obliterans. The idea that ulcer depends on diseased conditions of the blood vessel is supported by the observations in a few cases. Cases 21, 24 and 41 showed these vascular lesions. Cases 21 and 24 showed arteritis in the vicinity of the ulcer and the vessel filled with coagulated blood. Case 41 showed a perivascular

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19. Mayo, C., H.: Discussion of paper by G. K. Dickinson, J. A. M. A. 78: 1792 (June 10).

20. Stahr, H.: Intestinal Tumors in Children Caused by Trichocephalus, Deutsche med. Wchnschr. 48:1274 (Sept.) 1922.

desac. The edges were infiltrated and its appearance was that of a perforated ulcer of the stomach. The stomach, small and large intestines were opened. The mucosa of the entire digestive tract was normal.

CASE 45.—Autopsy was not performed. Operation revealed fecal material in the abdomen and a perforation of the sigmoid. The walls of the colon were described as rotten, and they only tore on attempts to suture. The author was unable to get a clear idea of the abdominal condition, but thinks the perforation probably resulted from thrombosis. Evidence in favor of stercoral or foreign body was scanty.

CASE 49.—Postmortem examination showed an ulcer in the transition of the rectum into the sigmoid flexure of the colon. Rupture was due to a so-called decubitus ulcer. The perforation orifice was found to contain a hard fecal mass.

CASE 50.—In the lower portion of the sigmoid there was a perforating ulcer the size of a bean, from which feces were discharged. The tissue in the vicinity of the ulcer was infiltrated, but not reddened. The ulcer was closed by five longitudinal catgut sutures; two rows were made. Sigmoidoscopy four weeks after operation showed the mucosa normal for 22 cm. Analysis of the foregoing eleven cases would rather tend to prove that the lesions were not due to diverticulitis.

Diverticulitis of the right half of the colon is rather a rare condition. In a study of twenty-seven cases, Giffen<sup>24</sup> found diverticulitis situated on the various segments of the colon as follows: Hepatic flexure, one; transverse colon, one; sigmoid, twenty-two; rectum, two, and anal ring one.

The ulcer may be the size of a pea or the size of a dollar. There are all variations in sizes between the two mentioned. They may be annular, or their long axis may be parallel with the long axis of the intestine. The description of the lesion in the various case reports differ. In some cases the ulcer is described as oval, round, irregular with sharply cut edges, circular, or they may appear to be punched out. The mucosa around the ulcer grossly appears to be normal and when the ulcers are multiple the mucous membrane between them is also normal, but, occasionally, there may be a secondary inflammation of the mucosa. There may be a chronic, diffuse, hypertrophy of the intestinal wall. The ulcer may be hard, indurated and resemble gastric ulcer. The base has been described as being yellow, gray or white. The depth of the ulcer is variable; sometimes it is shallow, involving the mucosa and submucosa alone or the muscle layer or the serosa may form the base of the ulcer. Often there is a marked overgrowth of connective and inflammatory tissue which, in the process of healing, contracts and may form an annular or longitudinal constriction, producing either partial or complete obstruction. Rarely, there is hemorrhage from the ulcer. Severe

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24. Giffen: The Diagnosis of Diverticulitis of the Large Bowel, J. A. M. A. 59:864 (Sept. 14) 1912.

that in the group of cases studied for ulcer the lesion tended to cause obstruction by a healed or healing stenosing cicatrix, while in diverticulitis there was no obstruction. In this group of patients obstruction was noted in ten cases. Hanseman<sup>28</sup> noted that false diverticula usually occur and are in close relationship to the blood vessels entering and leaving the intestine along the mesenteric border. This was not the case in this study; the ulcers usually occurred on the free border or anterior surface of the bowel, with the exception of case 17. A brief résumé of the gross lesion as studied by postmortem examination or at operation of ulcers of the sigmoid follows:

CASE 5.—Postmortem examination showed that the proximal part of the colon was tremendously distended, while the rectum was much smaller. On the lower portion of the sigmoid there was a hard, annular stricture. It was so narrow that a small pin could hardly pass through it. The intestine above the stricture was covered with feces. The stricture was formed by an ulcer, the size of a 5 franc piece. The base was narrow and the edges raw, thickened and hypertrophied. Cancer could not be detected. The patient died of intestinal obstruction.

CASE 8.—Postmortem examination showed six ulcers of the sigmoid. The ulcers were oval, resembling button holes and were all about the same size, and had the appearance as if the intestine was punched out. A certain number were perforated.

CASE 14.—Postmortem examination showed an oval perforation, 5 cm. wide and 1 cm. long, on the middle part of the sigmoid. The edges were sharp and sclerotic. The mucosa had disappeared around the perforation.

CASE 15.—Postmortem examination showed a perforating ulcer with sloping edges in the lowest portion of the sigmoid flexure. It opened into the abdominal cavity. There was a second ulcer beside it, which was ready to perforate. Its border was grayish.

CASE 24.—Postmortem examination showed a linear tear on the sigmoid about 2 cm. long and surrounded by a small layer of fibrin. On opening the colon, ulcerations were found on the mucosa. One of these ulcers was deep, almost annular, and had perpendicular edges. The linear perforation already described was found to be at the base of this ulcer.

CASE 25.—Postmortem examination was not made in this case, as the patient was cured following operation, and the lesion was not visualized, although the diagnosis of perforating ulcer of the sigmoid was made (see case reports).

CASE 36.—Autopsy was not performed. Operation revealed a perforation the size of a 50 centime piece on the anterior surface of the sigmoid. The edges were slightly indurated for a short distance, and beyond the induration, the mucosa of the colon was apparently normal. The edges of the perforation were resected, and the loss of substance was sutured in two layers. Although the peritoneum and the intestine did not appear to be inflamed, extensive drainage was instituted on account of a large amount of feces in the abdomen. The patient made a good recovery from this operation.

CASE 39.—Postmortem examination showed a small, round hole in the sigmoid from about 3 to 5 cm. in diameter, and about 12 cm. above Douglas' cul-

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23. Hanseman, D.: Arch. f. path. Anat. 144:400, 1896.





hemorrhage has occurred, but more often when the lesion is in the rectum, due to erosion of a blood vessel (cases 26, 47, 49 and my case 3).

In all cases, the initial lesion is acute, and an acute ulcer results. This ulcer may heal rapidly, but, on the other hand, it may extend, while a secondary inflammatory thickening occurs, corresponding in degree to the chronicity of the ulcer. A chronic ulcer, which is produced in this way, may likewise continue extending, so that a description of the ulcerative process comprises not only that of the formation of the initial lesion, but also that of the extension of acute and chronic ulcer.

However, the ulcer may continue as a chronic simple latent ulcer, giving rise to mild abdominal symptoms or, as stated before, may heal. The opposite course is perforation. From a study of this series of cases, it would seem that simple ulcer of the colon was rather prone to perforate; however, it is impossible to make this a definite statement since, in the majority of the cases studied, the diagnosis was only made when perforation occurred and it is likely that the simple latent ulcers go unrecognized. In this study of fifty-three cases, forty-two ulcers perforated and eleven did not perforate. The perforation is generally in the center of the ulcer which may be small or large. The omentum or a loop of adjacent bowel may tend to wall off and form a pocket, as in my case, one with an abscess resulting; this condition occurred in twelve cases; or the contents of the colon may be expelled into the general peritoneal cavity, giving rise to general peritonitis. The localized abscess resulting from a perforation often can be felt as a distinct tumor through the abdominal wall. The pus from this abscess may burrow and form sinuses into the liver, kidneys or any adjacent organ (cases 16, 17 and 18).

Vascular lesions about the ulcer, such as nonobliterative and obliterative endarteritis, thrombosis; complete obliteration by cicatricial fibrous tissue, penetrating into some of the capillaries have been described (cases 21, 24 and 26). There is an absence of epithelium and mucosa, and in some cases, of submucosa and muscularis. The layers lying underneath the destroyed ones have also lost their normal structure and given place to a cicatricial tissue, poor in cells but rather vascular. Ecot and Richard<sup>25</sup> found a direct infiltration of polymorphonuclear leukocytes and large phagocytic cells. There was also perivascular sclerosis.

Mintz<sup>26</sup> describes the serosa as considerably thickened with newly formed dilated vessels and a small round cell infiltration. He could not

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25. Ecot, F. C., and Richard, A.: Perforation of a Simple Ulcer of the Ascending Colon: Microscopical Examination, *Bull. et mém. Soc. anat. de Paris* 92:138, 1922.

26. Mintz, W.: Simple Ulcer of the Colon, *Zentrabl. f. Chir.* 50:1208, 1923.

the possibility of a perforation of the colon to be considered. The same perforation may be found to be the cause of localized peritonitis in other parts of the abdominal cavity. After a negative exploration of an organ, which is believed to be diseased, the surgeon should remember that a chronic ulcer or a perforation of the large intestine may exist in patients whose past history shows nothing with the exception of constipation, and he should make a careful examination of the walls of the colon.

It is of particular importance to differentiate, during an operation, between a pseudoneoplasm due to an ulcer, carcinoma and diverticulitis, since in cancer, the most radical treatment possible should be carried out.

#### TREATMENT

In order to discuss the rational treatment of patients with simple ulcer of the colon, chronic latent ulcer and perforated ulcer must be considered separately. Since this lesion has never been correctly diagnosed in the unperforated state prior to operation, it seems rather difficult to advise operation for the condition, even though a correct diagnosis has been rendered. In spite of the fact that only fifty-three cases have been reported in the literature, it seems that the lesion must be much more prevalent and goes unrecognized. The number of perforations that have been reported is relatively small in number, which makes me believe that the ulcer or ulceration must heal itself spontaneously rather often. A certain number of ulcers do perforate, and therefore operation, before this accident occurs, is rather a simple procedure and may be a life saving measure if the ulcer be a perforating one. Apparently, simple suture of the serosa over the base of a shallow ulcer is sufficient treatment, as proved in case 40 and in my case 2. When the ulcer has caused definite constriction, due to a healed contracting scar, a simple plastic operation may be sufficient rather than extensive resection. If, however, the ulcer, as a result of inflammation, has produced a pseudoneoplasm protruding within the lumen of the bowel causing definite obstruction, the usual resection of that portion of the bowel must be performed. The surgical treatment for persons with simple ulcer in the unperforated state may be divided as follows: (1) for simple shallow ulcer without constriction or obstruction, simply bringing the serosa over the base of the ulcer as reinforcement is sufficient; (2) for the constricting band due to a perfectly healed ulcer, a plastic operation is sufficient; (3) for an obstructing type of ulcer with secondary inflammation, the treatment must be resection.

The treatment in cases of perforated ulcer must be immediate operation. If the perforation is immediately visualized and opens directly into the peritoneal cavity, the ideal method would be to suture the perforation

shock is present, then to be followed by the usual signs and symptoms of general peritonitis as arises following perforation of any hollow viscus. 2. Ulcer of the colon sometimes forms an intra-abdominal tumor, owing to a small perforation which causes an extensive infiltration of the abdominal wall. There is a surrounding peritoneal reaction; adhesions of the small intestine or omentum form a true tumor which can be often felt. This type usually gives rise to localized pain and rise in temperature; if it is on the right side, like appendical abscess. There were twelve cases, about 22.5 per cent, in which a definite, palpable tumor could be felt (cases 19, 21, 24, 25, 27, 28, 29, 31, 39, 40, 48 and 51, and in cases 40 and 48, the ulcer had caused an intussusception. Occasionally, these symptoms subside due to a local, natural, defense reaction. The virulence of the invading organisms is lowered. The perforation is closed over by a layer of fibrin, then layer on layer of inflammatory tissue is deposited about the localized perforation. The temperature may become normal and even the pain may disappear, and the patient believes himself to be well. The inflammatory tumor persists however, and can be easily palpated. Essentially, the symptoms of perforated ulcer simulate those of peritonitis, either local or general.

#### DIAGNOSIS

The diagnosis of ulcer of the colon is difficult to establish before perforation has taken place. Simple ulcer of the colon has no pathognomonic signs by which the diagnosis can be made. In not one of the cases in the series studied was the diagnosis made before perforation or operation took place, with the exception of the case in which the ulcer was located in the rectum. Constant, fixed pain, associated with constipation, should make one suspect ulcer as well as cancer in the differential diagnosis. At best, this lesion can only be suspected, and, with the aid of the x-ray, the diagnosis may be made. The sigmoidoscope and proctoscope will be of considerable assistance when the ulcer is in the rectum, or low down in the sigmoid. X-ray examination will help to rule out a diagnosis of colitis and cancer.

When the ulcer has perforated and signs of peritonitis, either local or general, have made themselves evident, the diagnosis is usually made at operation. If an abdominal tumor can be felt, together with acute inflammatory signs, perforation of an ulcer should immediately be considered. The first impression is a perforated appendix, acute cholecystitis, volvulus, strangulation or intussusception, but whatever diagnosis is made, on account of the gravity of the symptoms, operation is usually performed at once. It is then that a knowledge of ulcers of the colon appears to be particularly valuable. In fact, in a peritonitis involving the right iliac fossa, the finding of a normal appendix should cause

There were approximately twice as many cases of ulcer of the colon in males as in females. This is not a disease of old age; the average proving that it occurs before middle life.

Perforations occurred in forty-two of the fifty-three cases reported.

#### REPORTS OF CASES FROM THE LITERATURE

##### CASE 1 (Marchesseaux,<sup>27</sup> 1837).—*Perforation of Ulcer of the Rectum.*

A woman, aged 45, an alcoholic with marked constipation, died of acute peritonitis. At autopsy, a stricture was found in the upper part of the rectum. Above the stricture, many grape seeds and fruit pits were found. The stricture barely permitted the passing of one's little finger. There was a large circular ulcer on its surface about 1 inch (2.5 cm.) wide; the edges were formed by slightly swollen, pale mucosa. The base was pale and was formed by the submucous connective tissue. In the center, a small perforation was noted. The intestinal coats were only slightly thickened. There was no evidence of ulcer in any other point of the gastro-intestinal tract. All the other viscera were normal.

##### CASE 2 (Rogee,<sup>28</sup> 1838).—*Chronic Ulcers of the Intestine Without Tubercular Perforation.*

A woman, aged 61, with a delicate constitution, for three years had been having frequent attacks of colic accompanied by nausea and vomiting. Diarrhea had not occurred. The condition gradually disappeared. She had no primary acute infection. She suddenly had violent pains in the abdomen and died with signs of peritonitis. At autopsy, the lungs showed evidence of old healed tuberculous process in both apexes. The viscera were normal. The peritoneum showed signs of acute peritonitis. There were six narrow ulcers in the last fifth of the small intestine opposite the attachment of the mesentery. The ulcers were elongated and their great diameter was perpendicular to the axis of the intestine. The base of some of the ulcers was formed by the peritoneum only; in others the base was formed by the muscle layer, and in some the submucous connective tissue formed the base. Granulations were not seen on the surface of the ulcers. Only one ulcer in the colon, situated high up in the rectum, perforated. It presented the same characteristics as the ulcers of the small intestine, but it was round and about the size of a 2 franc piece. The mucosa of the gastro-intestinal tract was normal with the exception of the ulcers. The mesenteric glands were normal and there was no evidence of tuberculosis present.

##### CASE 3 (Greenhow,<sup>29</sup> 1848).—*Perforating Ulcer of the Splenic Flexure.*

A man, aged 72, had an attack of renal colic six months before consulting a physician. Examination showed a calculus in the bladder. Lithotomy was performed on November 7. On November 9, slight abdominal pain, rapid pulse and marked constipation developed. Mild mercuric chloride was given on November 10; the patient grew weaker and had diarrhea, death occurred that morning. At autopsy, the peritoneum showed signs of peritonitis. The coats of the bladder were markedly thickened. The prostate was indurated and large. A small calculus

27. Marchesseaux: Stricture of the Upper Part of the Rectum with Old Ulceration, *Bull. Soc. anat. de Paris* 12:343 (Dec.) 1837.

28. Rogee: Chronic Ulcers of the Intestine Without Tuberculosis; Perforation; Acute Peritonitis; Death, *Bull. Soc. anat. de Paris* 13:181 (Aug.) 1838.

29. Greenhow: Perforating Ulcer of the Splenic Flexure, *Path. Soc. Newcastle and Calestead*, December, 1848.

without the excision of the edges, cleansing the abdominal cavity of fecal and purulent material and establishing adequate drainage. Certainly, resection would be contraindicated in the presence of a more or less generalized peritonitis. If the perforation has been walled off and a localized abscess has developed, incision, evacuation of the abscess, suture of the perforation whenever possible, without too much manipulation, and adequate drainage would be sufficient, rather than performing a more complete and dangerous operation.

When the ulcer is sufficiently low in the rectum, cauterization and tamponade is probably enough, as in case 26. In my case 3, tamponade was enough to check the hemorrhage, and the ulcer apparently healed itself.

#### SUMMARY

Fifty-three cases of simple, nonspecific ulcer of the colon are reported. Fifty cases were collected from the literature and three were personal cases. There were thirty-four autopsies, one incomplete autopsy and two deaths without autopsies in this series. Fifteen patients were cured as a result of operation; two of these patients had intestinal resections performed and the resected colon was studied grossly and microscopically. The others were studied only by visualization at time of operation. In one case, it was not stated as to whether the patient survived or not.

Simple ulcer, analogous to gastric or duodenal ulcer, may occur on any part of the alimentary canal from the esophagus to the rectum. Ulcer of the colon is a distinct and definite pathologic lesion which probably occurs more frequently than is suspected; the diagnosis usually being made only when the ulcer has perforated, or during an exploratory laparotomy or at the time of a postmortem examination.

Simple ulcer of the colon is usually the cause of the so-called inflammatory tumor or pseudoneoplasm and as a result of which, intestinal obstruction is produced either by the inflammatory tumor or constriction, usually due to a healing ulcer or the cicatrix of a healed ulcer.

The etiologic factor is probably not constipation and therefore stercoral or decubital ulcers are not common. Simple ulcer of the colon is not infrequently associated with gastric or duodenal ulcer. The fact that ulcer occurring on the stomach and on the first portion of the small intestine, namely, the duodenum, is accepted as having the same etiology, it is logical to believe that ulcer of the stomach occurring with an ulcer on another segment of the gastro-intestinal tract, namely, the colon, have the same etiology. Therefore, it seems that ulcer of the colon is probably a secondary and local manifestation of a general pathologic condition as gastric ulcer, and that the same etiologic factor may be the cause of simple ulcer on any segment of the alimentary canal.

a perforation of an ulcer of the sigmoid colon was found. This ulcer communicated with a closed pocket of cellular tissue as a result of the inflammation so that the fecal contents had not escaped into the free abdominal cavity and this explains the length of his illness.

CASE 7 (Claus,<sup>32</sup> 1856).—*Perforating Ulcer of the Descending Colon.*

A man, aged 47, had had typhoid twenty-five years previously and pneumonia fifteen years previously. On May 8, 1855, he had pneumonia again. On the seventeenth day of his illness, dyspnea increased and he had violent pains in his abdomen. He had diarrhea, followed by constipation which could not be relieved. He died two days after entering the hospital with evidence of peritonitis. At autopsy, on the lesser curvature of the stomach, an ulcer the size of a 5 centime piece was found and there were several other small ulcerations on the greater curvature. The small intestine was slightly hyperemic and contained four or five round worms. There was a rounded perforation the size of a 5 centime piece on the posterior wall of the descending colon and the edges were perpendicular. Nothing else was found in the gastro-intestinal tract. The lungs showed evidence of pneumonia.

CASE 8 (Dickinson,<sup>33</sup> 1867).—The patient was a woman, aged 42, who died in St. George's Hospital on Aug. 26, 1863. She said that she had had constipation and a bilious fever several months before admission. About a month before her death, she had pains in the left iliac fossa and died with symptoms of a circumscribed peritonitis. At autopsy, a cavity the size of a cocoanut was found in the left iliac fossa. This cavity was partly empty. The anterior wall of the cavity was formed by the abdominal wall and the posterior wall was formed by intestinal loops which were adherent to each other by means of solid lymphoid tissue. The cavity contained pus and feces, and communicated with the sigmoid by means of a certain number of perforating ulcers. About half a dozen ulcers were seen on opening the colon. The ulcers were oval, resembling button holes and were all about the same size. They were close together, parallel to each other and perpendicular to the long axis of the intestine. They did not present any thickening, and they had the appearance as if the intestine was punched out. The muscular layer was destroyed. There was no evidence of tuberculosis.

CASE 9 (Idem).—*Perforating Ulcers of the Descending Colon.*

The patient was a man, aged 42, who died at St. George's Hospital on Feb. 10, 1865. He had attacks of pain in the left hypochondrium for several years. These attacks have become worse recently. Pain was associated with constipation and he would be relieved by cathartics. The patient became edematous; his urine contained albumin and he had diarrhea which could not be controlled. This appeared to be the cause of his death. At autopsy, a large cavity filled with black feces was found. The cavity was made up of the diaphragm, spleen and descending colon. There were two small narrow ulcers in the upper part of the descending colon which opened into this cavity. There was no thickening of the intestinal coats. There was no other lesion present with the exception of the ulcers. These ulcers were in the form of button holes, close together, and parallel and their long diameter was perpendicular to the long axis of the intestine. No evidence of tuberculosis was found.

32. Claus, A.: Spontaneous Perforation of the Colon, Inaug. Diss., Zurich. 1856.

33. Dickinson: Perforating Ulcer of the Transverse Colon, Tr. Path. Soc. Lond. 18:101, 1867.

was found in the bladder. There was a large amount of feces in the left hypochondrium. There was a small perforation at the splenic flexure from which the intestinal contents escaped. The colon presented ulcers at a few other points. These other ulcers had almost penetrated through the entire thickness of the intestinal coats. Immediate cause of death was peritonitis due to perforation.

CASE 4 (Lebert,<sup>30</sup> 1861).—*Perforating Ulcer of the Colon.*

A man, aged 47, who had always been in good health, had sharp pains in the abdomen fifteen days before admission to the hospital. Pain was localized along the course of the colon. He became markedly distended, and later constipated. There was nausea and vomiting. On admission to the hospital, he had signs of peritonitis and died two days afterward. At autopsy, there was general peritonitis. The abdomen was filled with gas and there was a large amount of feces in the right iliac fossa. The lesser curvature of the stomach presented an ulcer about the size of a 5 centime piece, about 10 cm. from the cardia. The small intestine was normal. There was a rounded perforation a little larger than a 5 centime piece at the splenic flexure surrounded by an area of injection and false membranes. The ulcer when seen from the mucous surface showed the edges to be almost perpendicular.

CASE 5 (Idem).—*Ulcer of the Sigmoid; Intestinal Obstruction; Death.*

A man, aged 47, had always been in good general health, although he always complained of marked constipation and hemorrhoids. He continued to work until ten days before his death. At this time he began to vomit and became markedly constipated. In spite of all that could be done, the constipation persisted and his abdomen became more distended, but without pain. He was much nauseated and vomited continually until his death.

At autopsy, the abdomen was found to be markedly distended. There were only a few adhesions. The only changes were found at the lowest portion of the sigmoid. Above this point, the colon was tremendously distended while the rectum was much smaller. At this point, there was a hard annular constriction. The stricture was so narrow that a small pin could hardly be passed through. The intestine above the stricture was filled with feces. The stricture was formed by an ulcer the size of a 5 franc piece. The base was yellowish and the edges broad, thickened and hypertrophied. After careful examination with a microscope, cancer could not be detected. There was a single simple ulcer which had caused the obstruction of the intestine, by increasing hypertrophy of the intestinal walls.

CASE 6 (Dujardine,<sup>31</sup> 1864).—*Perforating Ulcer of the Splenic Flexure.*

A physician, who became suddenly ill with pain on April 12, described the pain like that of a sharp blow which caused him to sit down and rest. Shortly after, he was able to walk home complaining of a pain in the left hypochondrium. His physician made a diagnosis of colitis and applied leeches which seemed to give him relief. At the end of twenty days, he was advised to go to the country for a rest. He did not improve and complained of indigestion and pain. On returning, he consulted Prof. Orsey on June 5, who made a diagnosis of tumor of the spleen or adjacent organs and advised waiting until the next day because he wished to see the color of the patient's skin before he made his final diagnosis. He had several attacks of pain with diarrhea and fever and died on June 24. At autopsy,

30. Lebert: *Perforating Ulcer of the Colon*, *Traité d'anatomie et pathologie générale et spéciale*, 1861, vol. 2, p. 206.

31. Dujardine: *Perforating Ulcer of the Splenic Flexure*, *Soc. d sc. méd. et naturelles de Bruxelles*, September 5, 1864.



any tuberculous lesions. The mucosa stopped abruptly where the ulcers commenced. The objective appearance was that of a simple ulcer. The stricture at the splenic flexure was due to the cicatrix of a healed ulcer.

CASE 13 (Choupe,<sup>37</sup> 1870).—*Simple Ulcer and Stricture of the Large Intestine.*

A man, aged 32, had colic almost continuously for two months. He vomited after every meal, and colic returned after vomiting. The vomitus and feces were black. The patient was very constipated and would go for seven or eight days without a bowel movement; this condition would be followed by diarrhea. His appetite was good. At autopsy, there was no evidence of tuberculosis. There were signs of peritonitis in the abdominal cavity. The cecum and ascending colon were enormously distended. A stricture was situated at the hepatic flexure. Palpation at this area did not show any indurated tissue. After having incised the large intestine above and through the stricture, a large ulcerated area with irregular borders was found in center of stricture. No evidence of malignancy or any other lesion was found in the gastro-intestinal tract.

CASE 14 (Demange,<sup>38</sup> 1879).—*Old Perforation of the Sigmoid Flexure, Obstructed by Epiploic Adhesions; Rupture of These Adhesions; Acute Peritonitis.*

A man, aged 72, had sharp abdominal pains one evening, and was found dead the next morning. At autopsy, generalized acute peritonitis was found. There was an oval perforation 5 mm. wide and 1 cm. long on the middle part of the sigmoid flexure. The edges were sharp and sclerosed. The mucosa had disappeared around the perforation. The base of the ulcer was occupied by epiploic masses which were adherent to the edges and which undoubtedly formed a stopper up to the time of rupture.

CASE 15 (Mickle,<sup>39</sup> 1883).—*Double Perforating Ulcer of the Sigmoid Loop of the Colon.*

A man, aged 45, had an extremely severe pain in the right iliac region near the median line after having taken a purgative. There were signs of peritonitis due to perforation. He died twenty-four and a half hours after this sudden onset. Autopsy revealed generalized peritonitis. There was a perforating ulcer with sloping edges in the lower portion of the sigmoid loop. It opened into the abdominal cavity. There was a second ulcer beside it which was ready to perforate. Its borders were grayish. There was stenosis of the mitral valve and biliary calculi, but no calculi were found in the intestine or peritoneum.

CASE 16 (Bradbury,<sup>40</sup> 1884).—*Ulcer of the Cecum, Complicated with Abscesses of the Liver.*

A man, aged 30, was admitted to the hospital on May 28, 1884, with a condition, the first symptoms of which appeared on April 25 and consisted of abdominal pain on the left side, chills, vomiting, diarrhea, fever and loss of weight. On admission, there was dulness over the base of the left lung. The abdomen was soft but painful in the left iliac fossa. Cough was noted. Examination did not show the presence of a rash. There was an alternation of the chills and fever. The

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37. Choupe: Simple Ulcer and Stricture of the Large Intestine, *Bull. Soc. anat. de Paris* 45:322 (May) 1870.

38. Demange, E.: Old Perforation of the Sigmoid; Acute Peritonitis, *Rev. méd. de l'est*, August, 1897, p. 500.

39. Mickle: Double Perforating Ulcer of the Sigmoid, *Brit. M. J.* 1:637, 1883.

40. Bradbury: Ulcer of the Cecum, Complicated with Abscess of the Liver, *Lancet* 2:637, 1884.

CASE 10 (Robin,<sup>34</sup> 1869).—*Ulcer of the Descending Colon.*

A man, aged 66, entered the hospital on May 19, 1868. He had had gout since he was 19 years of age. On the morning of May 20, he had a severe attack of gout and there followed severe constipation for five days with slight abdominal distention. He was given a purgative, which caused one bowel movement. On May 26, the patient demanded his discharge from the hospital. This was refused on account of the increase in the abdominal distention. The constipation and distention increased. His condition became serious on May 29. There had not been any stools for several days. He now had a weak pulse, coldness of the extremities and vomiting. Galvanism was applied to the abdomen without results. It was impossible to pass an esophageal sound to the upper limit of the rectum. The patient's condition became much worse and death followed. At autopsy, the intestine protruded on opening the abdomen. The colon was distended with gas and liquid feces; its walls tore at the slightest traction. There was no evidence of peritonitis or strangulation. There was an ulcer the size of a 5 franc piece in the middle portion of the descending colon. The ulcer was of recent date. Nothing was found which could explain the arrest of the sound in the rectum. Crystals of sodium urate were found in the articulations of the toes.

CASE 11 (Costin,<sup>35</sup> 1870).—*Perforating Ulcer of the Ascending Colon.*

A man, aged 45, had had abdominal pain, constipation and slight fever. Palpation showed that the colon was filled with hard feces. Various purgatives such as castor oil, mild mercuric chloride, senna and croton oil were administered without any notable result. The patient died twelve days after he was first seen. At autopsy, the small intestines were found to be distended. There was evidence of peritonitis. There was a certain amount of exudate in the peritoneal cavity and it had a fetid odor. The right side of the omentum was gangrenous and presented small disseminated abscesses. There was an old ulcer with sharp borders on the posterior surface of the middle third of the ascending colon. It had perforated through the entire thickness of the intestinal wall. The other viscera were normal.

CASE 12 (Lepine,<sup>36</sup> 1870).—*Annular Ulcer of the Intestine; Perforation of the Small Intestine; Stricture of the Large Intestine, Autopsy.*

A woman, aged 70, died in the service of Dr. Charcot shortly after admission to the hospital. There was no clinical information. The abdomen was large, and the peritoneum was markedly injected. Several loops of intestine were covered with false membranes. The small intestine and the ascending and transverse colon were dilated, but the descending colon was of normal size. There was a stricture at the splenic flexure. The little finger could not be passed through this stricture. The intestinal walls were greatly thickened through the whole extent of the stricture. There was a round ulceration of small size a few millimeters above the stricture. The mucosa of the large intestine was normal throughout with the exception of the small ulcer. In the terminal ileum, there were six round ulcers penetrating to the muscle layer. The ulcer which was most distant from the ileocecal valve was 2 or 3 cm. in diameter, and the borders were thin. Careful examination showed that this perforation had not been artificially produced during autopsy and that it produced the terminal peritonitis. There was no evidence of

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34. Robin: Ulcer of the Descending Colon. Thèse Denaire. Paris, 1869.

35. Costin, J. G.: Perforating Ulcer of the Ascending Colon, Brit. M. J. 2: 247, 1870.

36. Lepine: Perforation of the Small Intestine; Stricture of the Large Intestine, Bull. Soc. anat. de Paris 45:27 (Jan.) 1870.

There was a continuous discharge of pus from the thoracic wound. The functions of the digestive tube were perfectly regular. The cachexia increased toward the end of May, and the patient died on June 2, 1886.

Autopsy showed that the head was normal, and the pericardium was distended with about 1 pint (473.2 cc.) of clear and limpid fluid. Pericarditis was not noted. The pleura were adherent and contained a cloudy liquid rich in fibrin. Examination of the lungs showed generalized bronchopneumonia with suppuration and formation of small disseminated abscesses. The left lung was in a worse condition than the right. Peritonitis was not found in the abdomen. The ascending colon was firmly united to the liver at the hepatic flexure. It formed one of the walls of the cavity filled with pus. This suppuration extended into the right lobe of the liver, which was softened and friable. It communicated with an opening in the right flank by means of a narrow fistula situated in the posterfor axillary line between the ninth and tenth ribs. There was only a small amount of pus. The tenth rib was necrotic at the level of the sinus. On opening the ascending colon, a small ulcer the size of a pea was found. It was evidently of old formation and had perforated the wall of the intestine and opened into the area of suppuration. The ulcer was circular and had rounded edges. It did not present any trace of active evolution. There was nothing to indicate the origin of this ulcer. The rest of the digestive tract was normal. The spleen showed amyloid degeneration. The kidneys were fatty and slightly amyloid. The pelvic organs were normal.

CASE 19 (*Idem*).—*Ulcer of the Colon and Cecum.*

A woman, aged 49, fell from a wagon on Aug. 14, 1887. She entered the hospital on August 16 for contusions of the face and the right thigh and abdominal pains. There was no history of previous abdominal disorders. Her general condition was grave. She was constipated for six days following the accident and had continual, greenish and aqueous vomiting. She had a profuse evacuation on August 20, undoubtedly due to a purgative; her stools were fetid and liquid; the vomiting ceased; she had fever; the diarrhea persisted. Examination of the urine did not show any albumin. On August 28, a diffused swelling was found at the hepatic flexure. The patient was weak and her temperature was normal. A tumor gradually developed and became of considerable size. It was situated at the hepatic flexure of the colon. There was a gradual weakness; the stools were irregular and were dark, fetid and liquid. On September 20, she had cough, pneumonic expectoration and fine crepitant râles at both bases. The diarrhea and cachexia continued, and the patient died on October 20. At autopsy, the heart and pericardium were found to be normal. The pleurae were also normal. The right lung showed hepatization of the base and disseminated suppuration. The left lung showed generalized bronchopneumonia and the bronchi were filled with pus. Chronic generalized peritonitis was found in the abdomen; the intestinal loops were adherent to each other. There was a collection of fecal matter and pus around the cecum and ascending colon. This collection extended upward as far as the diaphragm, passing in front of the liver. The pus and feces were contained in adhesions. There was a circular ulcer at the base of the cecum opposite its peritoneal insertion. This ulcer had rounded edges and had perforated through the intestine. It did not present any sign of recent evolution. It was the size of a 3 pence piece. A second similar ulcer, twice the size of that of the cecum, was found on the anterior wall of the ascending colon about 3 inches (7.6 cm.) from the cecum. There were no signs of typhoid, dysentery or tuberculosis. The intestines were soft and were in putrefaction. The right kidney showed congenital atrophy; it was the size of the kidney of an infant, while the left kidney was twice the normal size. The other abdominal viscera were normal.

abdomen became distended and painful on June 25, and the area of dulness around the liver increased. Acute pain developed in the right flank on July 9, and there was a large pleural effusion of the right side. The patient died on July 16. Autopsy revealed the right pleura filled with yellowish pus which had a nauseating odor. There was a fistula communicating between the pleura and an abscess of the liver. The liver contained many abscesses of various sizes, the largest of which was about the size of a lemon. This was the abscess which had ruptured through the diaphragm. There was an ulcer the size of a pea in the intestine near the attachment of the appendix to the cecum. It was surrounded by congested mucosa, but there was no perforation of the wall. There was no evident cause of the ulcer; the appendix was normal. The cecum was fixed in the right iliac fossa by old adhesions. The hemorrhoidal veins and the inferior mesenteric veins were filled with clots and pus. There were no lesions in the rectum or small intestine.

CASE 17 (Oliver,<sup>41</sup> 1895).—*Acute Perforating Ulcer of the Ascending Colon.*

At autopsy, there were two longitudinal ulcers in the colon  $2\frac{1}{2}$  inches (6.27 cm.) above the ileocecal valve. The larger ulcer was about 1 inch (2.5 cm.) in diameter, while the other scarcely admitted the tip of a goose feather. The surrounding tissues appeared to be normal as well as the tissue between the two ulcers. The two perforations were of rounded form and their edges were perfectly regular. The different tunics of the intestine had undergone necrosis to an equal degree; however, the muscle layer was retracted so that there resulted a prolapse of the mucosa which appeared to be redundant.

The larger opening, seen from the outside, presented the appearance of an artificial anus while the smaller opening could scarcely be discovered because of the retraction and the elasticity of the intestinal tissue.

The ulcers were situated exactly in the middle of the posterior surface of the ascending colon. The posterior surface, which was not covered by peritoneum, was lined by the connective tissue of the fascia which filled the lumbar space and the anterior surface of the right kidney. The necrosis had gradually extended through the intestinal wall, forming a tunnel through which fecal material escaped into the areolar tissue separating the colon and the right kidney from the subadjacent tissues. The peritoneum showed only slight signs of inflammation; only the lower edge of the liver presented traces of fibrinous exudate over a limited area.

CASE 18 (Parker,<sup>42</sup> 1887).—*Ulcer of the Ascending Colon.*

A girl, aged 18, entered the hospital on Sept. 16, 1885 for perityphilitis; she had been treated with rest and poultices. She improved and left the hospital in six weeks. On Dec. 24, 1885, she noticed a swelling in the right thorax redness, tension and dyspnea. The tumor increased in size; she coughed and expectorated. She returned to the hospital. The abscess was punctured on January 12, but only a half ounce (14.7868 cc.) of pus was obtained. An incision was made on January 13. The cavity was irrigated, but there was little pus. The patient's general condition improved at first and then became worse; cough, profuse expectoration, night sweats and hectic fever developed. At about the middle of February it was believed that there were signs of subacute pulmonary tuberculosis.

41. Oliver, J.: Acute Perforating Ulcer of the Ascending Colon, *Lancet* 1: 424, 1885.

42. Parker, A.: Ulcer of the Ascending Colon, *St. Barth. Hosp. Rep.* 23:213, 1887.

the cecum. The postoperative course was uneventful. The patient became cured and left the hospital on the fortieth day. He was in perfect health two and one-half months later and had gained 12 Kg. in weight.

Examination of the cecum showed that the tissue removed at operation consisted of the cecum, appendix, ascending colon, a part of the transverse colon and 2 cm. of the small intestine. The total length was 35 cm. The intestine was opened following along the external border. This incision divided a loss of substance into two almost equal parts at the level of the cecum. It was an oval ulcer with sharp outlines and the edges were about 2 mm. high. The base was indurated, pale gray and of uniform coloration. This ulcer was almost opposite the valve of Bauhin; its small vertical axis measured about 3.5 cm.; its great axis was in a transverse direction and measured 7 cm.; and the two extremities of this transverse great axis were each 1.5 cm. from the commissures of the ileocecal valve. The mucosa of the cecum was not absolutely normal; it appeared to be slightly infiltrated, and in addition, it presented white streaks which radiated from the edges of the ulcer. These streaks were almost fibrous and they flattened the folds of the mucosa, which was pink and shining. The mucous membrane of the intestine was normal in all of the other portions. The ulceration was in the middle of a large indurated plaque of almost cartilaginous hardness. This induration was situated on the antero-external and posterior walls of the cecum for a distance of about 7 cm. Its edges decreased in hardness and gradually disappeared. At the level of the induration, the intestine was considerably thickened and measured more than 1 cm. The intestine seemed to be of normal thickness in all other parts.

Microscopic examination at low magnification showed that the ulcer had destroyed the entire thickness of the glandular layer, the musculature of the mucosa and the most superficial part of the mucous membrane. The glands were increased in length about 5 cm. The connective tissue was much more dense than that of normal intestine; it formed tight, thick bundles which stained intensely with acid fuchsin. The muscular layers were hypertrophied; the internal layer measured 3 mm. and the external layer 2 mm. The serosa was also slightly thickened. Under higher magnification, it was found that in the vicinity of the ulcer the glandular layer was infiltrated in its entire thickness by a large number of embryonal cells. At certain points, these cells formed masses resting on the musculature of the mucosa. The epithelial lining cells of the intestine and those of the tubular glands appeared to be normal. The base of the ulcer was formed by the serosa; it was made up of connective tissue bundles irregularly sectioned by the ulcerative process. In the superficial parts especially, it was infiltrated by a large number of embryonal cells and at certain points there were small interstitial hemorrhages. Vascular lesions could be seen below the ulceration; certain arterioles showed obliterating endarteritis; others were thrombosed and filled with coagulated blood; finally there were larger vessels which presented slight traces of endarteritis. In many places the connective tissue around these vessels was thicker and tighter than elsewhere. The vascular lesions were far from being generalized; most of the arterioles subadjacent to the ulcer appeared to be completely normal. Sections of the colon above the ulcer showed that the coats of the intestine were normal and there were no vascular changes.

CASE 22 (Southam,<sup>45</sup> 1895).—*Perforating Ulcer of the Cecum.*

A man, aged 67, who had suffered from symptoms of incomplete obstruction of the intestine for several months, died suddenly a short time after admission to the

45. Southam: Perforating Ulcer of the Cecum, Brit. M. J. 1:254, 1895.

CASE 20 (Ollier,<sup>43</sup> 1892).—*Slough of the Cecum; Perforation.*

A man, aged 56, suddenly had a violent abdominal pain. There were signs of peritonitis and he died on the seventh day. Autopsy showed generalized peritonitis. There were two perforations of from 1 to 3 mm. in diameter, on the anterior surface of the cecum 2 or 3 cm. from the ileocecal valve. They were on the internal surface of the intestine in the center of a gangrenous area which was the color of dead leaves and was 5 or 6 cm. long and 1 to 1.5 cm. wide and surrounded by an area of inflammation. The rest of the intestine was normal and the appendix was intact.

CASE 21 (Morel and Secheyron,<sup>44</sup> 1895). *Ulcer of the Cecum; Inflammatory Pseudoneoplasm; Ileocecal Resection; Cure.*

A man, aged 46, entered the hospital on Sept. 17, 1895, for digestive disorders and progressive general weakness. He was tall and thin. On admission to the hospital, his face had an earthy tint, and his features showed a condition of general weakness. The disease began on July 14, 1895. Suddenly and without any cause, while working, he had had a severe pain in the right iliac fossa. Nevertheless, that day and the following days he had been able to continue working, but he had had almost continual pain. This pain presented exacerbations at fixed periods, coming on two hours after each meal. In the interval, there was rather a sensation of weight or heaviness at the level of the cecum, than a true pain. The digestive functions continued to be regular; there was no constipation or diarrhea. Stools were passed every day without increasing the pains and without discharge of blood and melenæ. His appetite remained excellent, but in spite of these conditions, he lost weight and strength.

From the beginning of the disease, the patient had noticed a swelling in the right iliac fossa. This swelling was situated between the anterior superior spine of the ileum and the umbilicus. Palpation was not painful, and showed an ill defined, elongated, lobulated tumor which was mobile in all directions. The dullness was not absolute on percussion. There were no adhesions to the skin. The glands in the groin were normal. In the presence of this tumor, and especially on account of the patient's straw-yellow color and earthy tint, a diagnosis was made of cancer of the cecum. The tumor seemed to be well limited, nonadherent, and surgical operation seemed to be justified. The patient was placed on a milk diet for eight days and he was given benzonaphthol to produce intestinal asepsis as much as possible. Another careful examination was made before giving the anæsthetic. A small tumor could be clearly felt at the upper part of the right iliac fossa. It was mobile and the size of a small apple. It seemed to be surrounded by a sort of resistant and lobulated tissue. After the patient was under the anæsthetic, it was impossible to palpate this tumor and only a diffuse swelling could be felt.

Operation was performed. Palpation of the abdomen showed a tumor which protruded into the cecum. This tumor was surrounded by an indurated zone which extended along the external wall of the cecum to 6 or 8 cm. from the valve. There was an oval, thickened plaque, about the size of a 2 franc piece, situated on the adherent border of the mesocolon 10 or 12 cm. from the valve. It was milky white. The mesenteric glands near the cecum were large and hypertrophied. The appendix was normal. The diagnosis at operation was cancer of

43. Ollier: A Case of Double Perforation of the Cecum, *Loire méd.* 11:3 (Jan. 15) 1892.

44. Morel and Secheyron: Ulcer of the Cecum: Pseudoinflammatory Neoplasm; Ileocecal Resection; Cure, *Soc. de méd. de Toulouse*, 1895.

and considerable gas escaped on opening the peritoneum. The true pelvis was filled with a cloudy, seropurulent fluid containing fibrinous false membranes. On examining the contents of the abdomen, one single loop of intestine was found to be of enormous size and was recognized to be a portion of the large intestine. It extended obliquely from the right iliac fossa to the left hypochondrium. On elevating it slightly, a linear tear about 2 cm. long and surrounded by a small layer of fibrin was found on the right lateral surface. Intestinal matter was escaping through this opening. Great difficulty was experienced in determining which portion of the large intestine was affected. However, it was evident that this distended loop was the sigmoid which had greatly increased in size and had left the true pelvis to extend into the abdomen in front of the viscera. After having extracted this loop from the abdomen, and after having sectioned it longitudinally, it was seen that it formed an enormous sac containing many kilograms of fecal material which was greenish brown, soft and did not contain scybala or foreign bodies. The intestinal walls were indurated and thick. Ulcerations were found on the mucosa. One of these ulcers was deep, almost annular and had perpendicular edges. The linear perforation already described was found at its base.

Microscopic examination, at low magnification, showed that the ulcer was funnel-shaped; the loss of substance occurred only in the mucosa and the musculature of the mucosa. The base of the ulcer was formed by the submucosa; the edges were perpendicular and were formed by the glandular layer of the mucosa and the musculature of the mucosa. One of the edges of the glandular layer was separated from the muscular layer which was destroyed, and at this level there was a free space separating this layer from the muscular layer. The other layers of the intestine were normal in appearance. Under higher magnification, it was found that the anatomic elements composing the glandular of the intestine in the vicinity of the edges of the loss of substance stained poorly; the nuclei of the glandular epithelial cells, as well as their protoplasm and the connective tissue of the wall of these glands had undergone coagulation necrosis. A short distance from the edges of the ulcer it was found that the anatomic elements preserved their normal structure. The base of the loss of substance was formed of loose connective tissue containing several round cells in its meshes; although the inflammatory process was relatively slight at this level, it was found, however, that this part of the submucosa contained many more embryonal cells than at other points of this tunic distant from the loss of substance. There was no appreciable ulceration of the vessels or the other layers of the intestine. In this case, the ulceration was chiefly due to necrosis of the superficial layers of the mucosa accompanied by a moderate inflammatory process in the subadjacent part of the mucosa.

CASE 25 (Gamgee,<sup>48</sup> 1898).—*Perforating Ulcer of the Sigmoid Flexure of the Colon.*

A man, aged 28, had ulcerative colitis in August, 1897. He suddenly had an acute pain in the inferior region of the abdomen on November 1. His temperature ranged between 100 and 101 F. for several days. A circumscribed tumor gradually developed in the left iliac fossa. The tumor was incised and about 3 drachms (11.09 cc.) of pus were obtained from a localized intraperitoneal abscess. Twelve days after operation, gas and the contents of an enema escaped through the wound. The fistula closed and the patient recovered.

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48. Gamgee: Perforating Ulcer of the Sigmoid, Brit. M. J. 1:950, 1898.



hospital. At autopsy, a stercoral ulcer was found on the posterior wall of the cecum. There was a small perforation at the center. The appendix was normal but the cecum and colon were distended by feces. The distention was apparently due to atony of the intestines, because there was no obstruction along the course of the intestine.

CASE 23 (Guinard,<sup>46</sup> 1896).—*Perforating Ulcer of the Hepatic Flexure of the Colon.*

A man, aged 27, while in good health, suddenly was seized with violent abdominal pain. Laparotomy was performed thirty-six hours later. There was diffuse peritonitis. The appendix was simply congested, but was excised; its cavity was free. The patient died thirteen days after operation. At autopsy, there was a purulent area containing gas at the junction of the ascending and transverse colons. The omentum was thickened and black. There was generalized peritonitis at the hepatic flexure and a perforation the size of a 5 franc piece was found. The intestinal mucosa was greatly congested. No other ulcers were found in the digestive tract. The perforation of the colon was the primary cause of the symptoms.

CASE 24 (Morel and Rispaïl,<sup>47</sup> 1896).—*Ulcer of the Pelvic Colon; Perforation.*

The patient was a man, aged 67, who entered the hospital on April 26, 1896. His hereditary history was negative. He had never been seriously ill; however, since infancy, he frequently had dull pains in the abdomen, undoubtedly due to chronic constipation; his stools had never been regular and at times he had profuse evacuations of solid material. At the time of the first examination, constipation had lasted for one month. During this time, the patient had no desire to go to the stool. His appetite was preserved. Food did not produce any discomfort or sensation of weight; he had no fever and his facies were not altered.

Examination showed that the abdomen was large and tense. A tumor of cylindrical shape could easily be seen under the skin. It began in the cecal region, ascended obliquely and became lost in the left hypochondrium. Palpation showed that this swelling was hard, resistant and of uniform consistency throughout its whole extent. Percussion showed marked loss of resonance. The left side of the abdomen seemed to be effaced in contrast to the distention of the right side. On palpation, it seemed that the sigmoid and the descending colon were empty, and over these regions percussion gave the usual abdominal resonance.

Rectal examination did not show any tumor or stricture. The fingers seemed to penetrate into a sort of excavation, as if the rectal ampulla was dilated in all directions. It was completely empty and did not contain any fecal matter. On account of these different symptoms, a diagnosis was made of intestinal occlusion. Although the distended loop extended obliquely upward and to the left, and did not follow the course of the ascending and transverse colons, it was believed that the cause of the obstruction was at the splenic flexure. The nature of the obstacle could not be determined. Cancer was eliminated. The patient was placed on a milk diet and a purgative enema was given on the 22d. Castor oil was given on the 23d and repeated on the 24th; three stools. On the 25th, he had a spontaneous stool. There was pain at the level of the umbilicus, which soon radiated. He did not vomit. Death occurred suddenly on the 26th. The patient had refused any operation. At autopsy, the abdomen was greatly distended

46. Guinard: *Perforating Ulcer of the Hepatic Flexure*, Thesis Paris, June, 1896, no. 324.

47. Morel and Rispaïl: *Ulcer of the Sigmoid; Perforation*, Soc. de méd. Toulouse, 1896.



several capillaries, although the lumen was perfectly outlined by the elastic membrane and the middle tunic. The presence of cicatricial tissue containing vessels in the interior of an artery can only be interpreted as representing an old thrombosis of this vessel.

**CASE 27 (Tedenat,<sup>49</sup> 1902).—*Enormous Retrocecal Abscess; Multiple, Large Perforations at the Origin of the Colon; Secondary Suture; Cure.***

A man, aged 40, who had had good health up to the age of 26 years, while living in Brazil for four years, had had syphilis, malaria and beriberi; he drank alcohol to excess. He returned to France in 1889. He had chronic constipation with abdominal pains, frequent cough and was only in fair general condition. The present disease began on April 29, 1901, with sudden pains in the entire right side of the abdomen, radiating toward the thorax and groin, without vomiting, and without complete constipation. He remained in bed for twenty days with thirst and fever. His abdomen was slightly distended and was painful and tender on the slightest pressure.

The patient entered the hospital on May 21. He was pale and thin. His temperature was 40.2 C. (104.3 F.), and his pulse rate was 104 and small. There was sharp pain in the entire right half of the distended abdomen. The skin over the right iliac fossa was red. The cecum was distended and gave a dull tympanitic sound. Cough was paroxysmal and there was induration of the right apex.

Operation was performed on May 22. Roux's incision for appendicitis was made. The abdominal wall was indurated and bled freely. As soon as the peritoneum was opened, about 500 cc. of thick fetid pus mixed with gas and fecal matter escaped. The cecum was greatly dilated and was reddish-violet. There were grayish, false membranes on its antero-external surface, which was adherent to the parietal peritoneum. The appendix was of almost normal appearance and was found underneath the false membranes. On passing the finger behind the cecum, a large glassful of pus escaped. There were two rounded perforations, 12 and 15 mm. in diameter on the posterior surface of the colon a little above its origin. These perforations were about 3 cm. apart. At 4 cm. above the highest perforation, there were three other rounded perforations in a row, from 7 to 8 mm. in diameter. Two large rubber drains were placed behind the cecum and the entire perforated portion was surrounded with iodoform gauze and a large cotton dressing was applied. The patient passed a good night and on the next morning was much better; the temperature was practically normal; the pulse rate 69, and weak. On June 26, the patient's general condition was good. The fecal fistula still discharged. It was decided to close the fistula.

An operation was performed under chloroform. An incision 26 cm. long was made parallel to the first incision at one finger's breadth from the parietal fistula. The cecum was reached and the colon was separated from the abdominal wall. The intestine was almost normal. There was practically no change in the perforations on the posterior surface of the colon. Each of the perforations was closed with a purse-string suture, and the suture line was covered with peritoneum. A large rubber and gauze drain was inserted to keep the cecum and colon away from the incision. Dressings were made with compresses moistened with salt solution. In the evening, his temperature was practically normal; his pulse rate 98, and strong.

The patient left the hospital on July 26 with a granulating wound about 6 cm. long and from 1 to 2 cm. wide. The fistula closed. The intestine was not distended. There was no pain. The patient had a good appetite; his bowel move-

49. Tedenat, quoted by Quenu and Duval.

CASE 26 (Quenu and Duval,<sup>4</sup> 1902).—*Simple Hemorrhagic Ulcer of the Rectal Ampulla.*

A woman, aged 50, entered the hospital for profuse rectal hemorrhages. The hereditary history was negative. She had three children, two of whom died of diarrhea and convulsions; the living child was 16½ years of age. There had also been two miscarriages. She had been treated for metritis after the first miscarriage, and had been sent to mineral springs. She had not had any other illnesses. The digestive tract functioned normally; digestion was good; she did not have diarrhea or constipation. The stools were normal and did not contain any mucus or membranes. She used alcohol somewhat to excess. The first rectal hemorrhage occurred in November, 1899. It appeared without any definite cause and was profuse. She had syncope, and her pulse became weak. A subcutaneous injection of salt solution became necessary. The second hemorrhage occurred in May, 1900; it was arrested by rest in bed and ice. She became weak. In July, 1900, there was a third hemorrhage accompanied by syncope, which was controlled by ice and rest in bed. The fourth hemorrhage occurred in July, 1901; ice and rest in bed were instituted as before. The fifth hemorrhage occurred on May 25, 1902. This was perhaps the most severe hemorrhage, and rapidly caused syncope. Two injections of aqueous extract of ergot and an injection of salt solution were given. On the following day, the patient did not have hemorrhage. The urine did not contain sugar or albumin.

She entered the hospital on June 22. Rectal examination showed only some anal varicose veins. With the speculum 8 cm. above the anocutaneous line at the junction of the posterior wall with the right lateral wall, the following was found: (1) a superficial ulceration with a pink base, 5 or 6 cm. long, from which the hemorrhage occurred; (2) a cicatricial band situated just to the side of the ulcer which bled easily. The ulcer was cauterized with the thermocautery on June 22, and the hemorrhage ceased. Tampons were placed in the rectum. Menstruation commenced on the afternoon of June 23, and during the night there was a severe rectal hemorrhage which required salt solution. The uterine hemorrhage soon ceased. Tampons were placed in the rectum. The ulcer was on the road to cicatrization on June 27, and on July 12 healing was complete and the patient left the hospital.

Microscopic examination revealed an ulcer of the rectal ampulla with arterial thrombosis. Serial sections were made following the axis of the extirpated ulcer. On each side of the sections it was found that the rectal mucosa had an absolutely normal cylindrical epithelium. On the base of ulcer, the epithelium and the mucosa were lacking. In their place there was a depression 1 mm. deep and 1.5 mm. wide. The base of this depression was formed by a fibrous zone rich in migratory cells (especially phagocytes) and covered with many red cells. It also contained some smooth muscle fibers which seemed to belong to the muscularis of the intestine. This fibrous zone rested on a dense, sclerous, cicatricial tissue which contained few cells and was intensely stained by fibrous tissue stains. This tissue not only formed the deep portions of the ulceration, but it extended on each side below the mucosa which rested directly on it without the interposition of a muscularis mucosa or any of the other layers of the intestine. The mucosa was thinner than normal and its interstitial tissue contained many leukocytes. The cicatricial sclerotic tissue contained a large number of capillaries. In addition, it surrounded a certain number of small veins and arterioles. The largest of these arterioles presented a remarkable disposition. It was found that in all sections the lumen was completely obliterated by a cicatricial fibrous tissue containing



ments were regular and his general condition good. Tuberculous granulations were not seen either around the perforations or on the peritoneum. There were no lesions resembling cecocolic tuberculosis of the hypertrophic form. Hence, tuberculosis may be eliminated as a cause of these rounded perforations with perpendicular edges. Can the lesions be attributed to syphilis? The syphilis had been well treated.

**CASE 28 (Idem).—*Retrocecal Abscess in the Iliac Fossa and in the Fatty Tissue Around the Femoral Vessels in the Middle Part of the Thigh; Perforation of the Posterior Wall of the Cecum; Appendix Little or not Diseased; Death Due to Chronic Septicæmia.***

A man, aged 52, of good health, had had typhoid at the age of 18 years. On Aug. 10, 1891, after eight days of complete constipation, his abdomen became painful and he began to vomit. His condition was serious for four days and was attributed to intestinal obstruction. An enema produced a profuse evacuation. The same painful symptoms recurred on September 8. The maximum pain was in the right iliac fossa with radiation to the thigh. He did not vomit. There was an abundant discharge of gas through the anus. The stools became normal at the end of a week and the abdomen returned to its normal size, but the pain persisted in the iliac fossa and right thigh. He had continuous fever. A physician was called on September 20, and found a deep swelling in the iliac fossa extending to the middle part of the antero-internal surface of the thigh. The swelling increased progressively, remaining deep in the abdomen and becoming more superficial at the internal surface of the thigh. The patient entered the hospital on Oct. 12, 1891, thirty-four days after the beginning of this second attack. Although he continued to take milk and bouillon without vomiting, he was pale, thin, feeble and had hectic fever. There was a deep induration in the right iliac fossa. It extended to the median line without any marked redness of the skin and continued downward to the middle part of the thigh, elevating the vessels and thrusting them inward. The skin was red and adherent over the swelling in the thigh and showed fluctuation. There was an enormous edema of the entire leg. The intestine was moderately distended, but the abdomen was only slightly painful on pressure, except in the iliac fossa.

On October 13, an oblique incision 8 cm. long was made a little outside of the resonant protrusion formed by the cecum. Several adhesions were broken at the infero-external part of the thickened cecum and about 1 liter of fetid pus escaped. There was a perforation about 2 cm. in diameter on the external part of the posterior surface of the cecum. The purulent cavity was prolonged downward toward the true pelvis. A second incision was made 2 cm. below the crural arch. It was 6 cm. long and was parallel to and outside the femoral vessels. A counter opening was made behind the middle part of the tendon of the fascia lata. The crural focus communicated with the iliac focus through the crural canal. The cecum was adherent to the anterior abdominal wall. The purulent cavity was subperitoneal. The appendix was searched for in vain. Four drains were inserted. There was great improvement of the general condition for about twelve days. The patient took 2 liters of milk, bouillon and wine.

On October 25, there was a profuse discharge containing fecal material. The pains increased and the fever rose. Two days later, an incision of 5 cm. within and parallel to the first was made in order to reach the internal surface of the cecum, for the purpose of searching for another abscess, resecting the iliac portion or making an anastomosis. Some thin adhesions were separated. The appendix was practically free and was of normal appearance. It was found behind the cecum. It was rapidly resected. The operation had to be discontinued

the size of a 5 franc piece was found. This perforation was almost round and was situated on the antero-external wall of the ascending colon and was parallel to the axis of the intestine. The mucosa was invaginated. The appendix was adherent, but did not show any perforation. The perforation was excised and sutured. The patient's general condition improved, but the local condition did not show any improvement. The third operation, a median laparotomy with a transverse incision, was performed on July 18. The ascending colon was freed of numerous adhesions. Resection of 10 cm. of intestine with terminoterminal anastomosis. She was cured on August 7.

CASE 31 (Lyle,<sup>1</sup> 1912).—*Simple Ulcer of the Colon; Perforation.*

A woman, aged 26, was admitted to St. Luke's Hospital in October, 1909, with the diagnosis of acute appendicitis, with abscess. The history and clinical symptoms on admission appeared to be those of an acute suppurative appendicitis engrafted on a chronic appendicitis. On admission, her temperature was subnormal and the pulse rate, 92. A blood count showed 25,000 white cells, with 86 per cent of polymorphonuclears.

An incision was made over the mass, and a large abscess containing fecal matter was evacuated. On the inner wall of the cavity, about 2 inches (5 cm.) above the cecum, there was a large, oval, indurated ulcer, in the center of which was a perforation, with necrotic edges. The edges were trimmed, a section removed for examination, and the perforation was closed. The appendix was outside of the cavity and apparently had nothing to do with the condition, but as it might have been the source of the infection, it was removed. A small rubber dam drain was inserted and the wound was closed. The patient made an uneventful convalescence, and left the hospital twenty-three days later. Microscopically, the appendix showed nothing abnormal, and the section from the ulcer showed it to be a simple ulcer of the colon.

On March 12, 1912, the patient returned to the hospital for the correction of a ventral hernia springing from the scar of the former operation. When this operation was performed by Dr. Gibson, the only evidences found of the former ulceration were a few fine adhesions on the colon. The picture presented by the original condition was so striking that one might have believed he was dealing with a gastric perforation. After the operation, a more detailed history was obtained, and it was then learned that the patient had long been a sufferer from indefinite gastric symptoms. She had made the rounds of the clinics, and her condition had been variously diagnosed as ulcer of the stomach, gallstones, floating kidney, chronic appendicitis and cancer.

CASE 32 (Eunike,<sup>51</sup> 1918).—*Simple Ulcer of the Colon.*

Louis Sch., aged 53, was admitted to the hospital on Feb. 28, 1918. His past history showed that an operation for double inguinal hernia had been performed several years previously, the right side being operated on first. The condition had recurred. The patient had always had difficulty in having bowel movements. He was often very constipated. Of late, he complained of severe pain in his abdomen. Eleven days before admission to the hospital, he began to have severe attacks of pain. His bowel movements were irregular and thin. For the past three days, he had been vomiting.

Physical examination revealed a strong, well nourished man, with a full, strong and regular pulse beat. Marked tenderness was elicited in an area over the

51. Eunike, K. W.: Ulcer Simplex of the Colon, *Deutsche Ztschr. f. Chir.* 147:284, 1918.

débris was eliminated in seven or eight days, and a large intestinal fistula became established. The general condition of the patient improved rapidly, but the fistula still discharged abundantly.

On March 16, operation was performed for the cure of the artificial anus, under an anesthesia of a mixture of alcohol, chloroform and ether. A flap of skin 6 cm. long and 3 cm. wide was excised. There was a slight prolapse of the intestinal mucosa. It was separated with difficulty, inversed and sutured with a Lembert suture. The tissues were friable. The principal perforation was rounded and 2 cm. in diameter. Above this perforation there were two others, slightly smaller, separated by bridges of intestinal wall 1 to 2 cm. wide. These perforations were located at the origin of the colon. A resection of the ileocecal segment with partial resection of the colon was decided on. The lower end of the parietal incision was enlarged downward and inward and the upper end directly upward. The cecum was separated, drawn outside the wound with the terminal portion of the ileum and the first 10 cm. of the ascending colon. Forceps protected by rubber were applied on the colon 8 cm. from the ileocecal valve and on the ileum at the same distance from its opening into the cecum. A wide, lateral anastomosis was made between the ileum and colon over a distance of 5 cm. The terminal sections of both ends of the intestine were sutured. The edges of the wide and thick mesentery of the large intestine were sutured. All of these sutures were made rapidly with Lembert sutures of fine silk. The intestinal wall was sutured in three layers with the exception of a distance of 2 cm. through which a drain was passed to the line of intestinal sutures. A compressive dressing was applied.

On May 4, the patient was considered cured. He had a good appetite and digestion was easy. The stools were regular. The general condition was excellent and he had gained weight. Examination of the tissue showed that the cecum was congested; the wall slightly thickened, but there were no traces of ulceration of the mucosa. The ileocecal valve was soft. The three perforations were spread out over an extent of 6 cm., beginning at the origin of the colon. They were rounded and had a punched out appearance. The edges were slightly thickened and indurated. There were no traces of cancer or tuberculosis. The appendix was 8 cm. long, straight, regular in size and normal; its walls were soft. There were no adhesions, ulcerations or scars. The excised skin was thickened by a simple chronic inflammation. There was infiltration of leukocytes with bands of sclerotic connective tissue.

CASE 30 (Zickler,<sup>50</sup> 1910).—*Perforation of the Ascending Colon.*

The patient was a woman, aged 25, without any previous history. She had had her first child a month previously. The confinement was normal. On May 25, while in the toilet, she had a sudden violent pain in the lower part of the abdomen which soon decreased, but later reappeared with greater intensity and was accompanied by vomiting. She entered the hospital thirty-six hours after the onset of symptoms. On admission, she had symptoms of peritonitis and diagnosis was made of appendicitis.

Laparotomy was performed on May 27. On account of the serious condition of the patient, nothing could be done except to remove the feces in the abdominal cavity and drain. Her condition improved a week after the operation. A second operation was performed on June 2. The pus pocket was cleaned, and a perforation

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50. Zickler: Perforation of the Ascending Colon. *Beitr. z. klin. Chir.* 67:181. 1910.

believed that he had an intestinal obstruction in all probability due to cancer of the larger intestine. On admission to the hospital, he was in bad general condition; his complexion was earthy, his features drawn, and slight jaundice of the conjunctiva was noted. The pulse rate was about 100; the temperature, 38.5 C. (101.3 F.). Since his admission, the patient vomited several basins full of greenish fluid. His abdomen was distended, tense and was extremely painful throughout. The slightest pressure produced contraction of the muscles. There were no peristaltic contractions of the intestine. The arrest of feces and gas had been progressive and seemed to be total. It was thought that he had an occlusion due to cancer, but considering the condition of the patient, his temperature, the sharp pains on palpation and finally the appearance of the vomitus, it was suspected that this neoplasm was accompanied by inflammatory phenomena.

A median laparotomy was performed. When the abdomen was opened, it was seen that the intestinal loops were dilated, red and adherent to each other by means of fibrinous adhesions. The entire abdomen was carefully explored, and it was found that the right edge of the omentum was thickened and indurated and extended toward the right iliac fossa. It was adherent to the anterior wall of the ascending colon at its origin. It was carefully raised and was easily detached allowing the upper surface of the large intestine to be seen. Just above a line passing through the upper border of the intestine at its opening in the cecum, there was a regular circular perforation the size of a 50 centime piece. Its edges were sharp, hard and was located in the middle of a small indurated zone. This perforation was immediately closed with a tampon, and an incision was immediately made in the right iliac fossa, through which the portion of the large intestine on which the ulcer was situated was exteriorized. The exteriorization was maintained by fixing the intestine to the abdominal wall by means of several catgut sutures. This was done to gain time as the patient was already weak, and it was believed that the cecoiliac fistula thus established would have a good effect on both the peritonitis and on the intestinal obstruction. The intestinal loops were cleansed with ether through the median incision, and the operative incision was closed. A large drain was placed in Douglas' culdesac. Unfortunately, the patient died during the night following operation. The large intestine was removed at the autopsy. It presented no other lesion except the perforation which was situated at the origin of the colon on its anterior surface. The mucosa of the ascending colon and cecum seemed to be normal. With the exception of the induration which surrounded the ulcer, which was of slight extent, no other alteration of the intestinal wall could be found. The specimen was sent to a laboratory for examination, but unfortunately was lost so that no histologic examination could be made. Macroscopic examination showed that this perforation was distinctly different from those seen in ordinary ulcerations of the intestine and no lesion was found which could explain its production.

CASE 35 (*Idem*).—*Perforation of the Cecum.*

A youth, aged 20, was admitted to the hospital on Jan. 20, 1903, for appendicitis. He was operated on for an abscess of appendicular origin on February 25. A right lateral incision was made along the external border of the right rectus muscle. As soon as the peritoneum was seen, it was evident that pus would be found; in fact, on opening the abdomen, a creamy greenish pus with fecal odor escaped. After having sponged this pus, it was found that the intestinal loops were adherent to each other. The hand was passed along the abdominal wall until the posterior wall of the cecum was reached. At this time bubbles of gas

abdomen, which was tympanitic. Both herniae recurred. On the right side, there was a small recurrence and a light, pale small operative scar. The left hernia was about the size of a man's fist and was irreducible and tense. A diagnosis of strangulated left hernia was made.

An operation was performed on the left hernia under local anesthesia. The whole sigmoid flexure was tied down with adhesions and the wall was markedly hypertrophied. The incision was enlarged, and gas anesthesia administered. On enlarging the incision, there was a fibrous exudate, the form and color of which resembled that coming from a perforated ulcer of the stomach. Under deep general anesthesia, the hernia was repaired and an incision was made from the xyphoid to the navel. Again appeared the fibrous exudate. The stomach was found to be normal, but on the hepatic flexure a perforation could be seen. The wall of the bowel was much infiltrated. The perforation was sewed with considerable difficulty. The ligatures were cutting through. Tamponade and drainage was instituted. The patient made a good immediate convalescence, but died on the fifth day after the operation. Autopsy showed general peritonitis. The sutures on the hepatic flexure held. In the close proximity of the perforation, there were three or four small ulcers. The rest of the colon did not show any signs of a pathologic process. The whole large intestine was hypertrophied.

CASE 33 (Soupault,<sup>8</sup> 1920).—*Perforation of a Simple Ulcer of the Colon.*

A woman, aged 22, was admitted to the hospital suffering from abdominal disturbances of acute onset. The diagnosis of appendicitis had been made, with the surmise that in the course of an acute attack with remission, perforation had occurred some hours before the patient's entrance.

Operation was performed, the Roux incision of 10 cm. being used. Incision of the peritoneum promptly revealed on the anterior aspect of the presenting coil, a perforation the size of a small pea, from which fecal matter escaped. The perforation was immediately closed with forceps, and the intestinal coil (cecum and ascending colon) was gently wiped off with a moist compress. The perforation was found to be situated on the antero-internal border of the ascending colon, 10 cm. above the cecum. The rounded perforation measured from 4 to 5 mm. in diameter. The borders were slightly thickened and ecchymotic. The surroundings were slightly swollen and edematous, but not indurated. The intestinal wall was flaccid and hyperemic. The peritoneum had lost its normal sheen and presented a few false membranes. The appendix, lying in the focus of peritonitis, was not seriously affected, but was resected. The perforated ulcer was rapidly sutured with linen thread purse-string suture; a second seroserosus layer was closed by a U suture. The coils were irrigated with ether and two drains were placed in Douglas' space and in the iliac fossa, respectively. The wall was closed in two layers. The operative procedure took thirty minutes. The patient made a good recovery.

CASE 34 (Bazy,<sup>22</sup> 1920).—*Perforation at the Origin of the Ascending Colon.*

A man, aged 65, was brought to the hospital with symptoms of progressive intestinal occlusion. He had been having violent pains in the abdomen for eight days. He experienced severe colic which was generalized over the entire abdomen. He vomited. For two or three days, there had been the complete arrest of feces and gas. Interrogation of the patient showed that he had had intestinal disorders for a long time, and on several occasions he had presented painful crises accompanied by vomiting. He had chronic constipation. For these reasons, and considering the age of the patient, the physician who sent him to the hospital



was situated 3 cm. above the insertion of the appendix. The appendix was normal as well as the rest of the large intestine. The perforation had allowed fecal matter to pass into the peritoneum, and especially beans of which the patient had eaten a large quantity twenty-four hours before the beginning of symptoms. The edges of the ulcer were indurated and it had the appearance of an old lesion. The patient was a heavy eater and had chronic constipation. For three months he had been having discomfort in the right iliac fossa.

**CASE 38 (Lardennois,<sup>55</sup> 1920).—*Spontaneous Perforation of the Cecum.***

A man, aged 52, gave a past history which showed that he had had lead colic during the previous year, which had appeared while he was working on storage batteries. In addition, he presented evident signs of lead poisoning. Later, he suffered from digestive disorders and anorexia, difficult digestion and constipation. On September 9, while walking to work, he suddenly had a severe pain in the right iliac fossa and had to be taken home. A short time later, nausea and vomiting occurred. According to the patient's story, the right iliac fossa was extremely painful and the vomiting persisted. There was no evacuation of feces or gas. His condition improved slightly after several days, and on September 12 he took a purgative. He had several stools following this purgative, but the symptoms rapidly became worse and he was brought to the hospital during the night of September 16 in a dying condition. On admission, it was found that he had peritonitis. A median laparotomy was performed. Cloudy fluid was found in the entire abdomen. There were abundant false membranes. There was a circular perforation with sharp edges about 5 mm. in diameter on the cecum. It was at the most protruding portion of the antero-internal wall and appeared to be larger at the level of the mucosa than at the serosa. The appendix seemed to be normal. The cecal opening was rapidly closed. The appendix was removed for examination. Inspection of the abdomen did not show any other lesion. There was no other ulcer, nor was cancer perceptible on careful examination. The adhesions were liberated, and the intestines were washed with ether. Drainage was instituted. The patient died during the course of the following night.

A later examination showed nothing more than was found during the operation. The appendix did not present any lesion other than those of superficial congestion due to its presence in an area of peritonitis. Histologic examination was not made.

**CASE 39 (Schoemaker<sup>56</sup>).—**In 1906, the author treated a man who had been sick for five days. The patient had always been in good health previous to this time. On Sept. 12, 1906, he suddenly had a sharp pain in the abdomen which was followed by vomiting. At first the pain extended over the entire abdomen, but little by little it became localized in the lower part. The pain diminished in intensity while his general condition became worse. He was sent to the hospital on September 17. On admission, his appearance was bad. He had a characteristic peritoneal facies. Rectal examination showed that Douglas' pouch was distended and painful. The diagnosis was acute appendicitis (low appendix which had perforated and had given rise to an abscess in the true pelvis).

An incision was made in the median line from the symphysis almost to the umbilicus. On opening the peritoneum, a large amount of fetid pus escaped. The cavity was emptied and dried with gauze tampons. The loops of small intestine were adherent to each other. The appendix was found. It was red like the intes-

55. Lardennois: Bull. et mém. Soc. de chir. de Paris 46:447, 1920.

56. Schoemaker, quoted by Soupault.

were seen to arise, and at the same time the characteristic noise of intestinal perforations was heard. The appendix was twisted on itself and adherent, but there were no special lesions. On the other hand, a certain distance away from it on the anterior surface of the cecum was found a circular perforation which easily admitted the tip of the index finger. This perforation was easily closed by a double line of silk sutures. The appendix was removed. A drain was left in the abdominal cavity. The abdominal wall was closed in three layers. The patient left the hospital, cured, on April 7, 1903.

CASE 36 (Gregoire,<sup>53</sup> 1920).—*Perforation of an Ulcer of the Sigmoid.*

A man, aged 55, of robust constitution but with chronic constipation, had passed stools on several occasions which contained blood. He attributed this to hemorrhoids. On June 1, 1919, while walking, he had pains in the lower part of the abdomen and was obliged to go home. He thought that constipation was the cause of the pain, and he took an enema. When he went to the toilet, he suddenly had a violent pain with vomiting. There was violent colic. He went to the hospital seven hours later. On admission, he was in great pain but his general condition did not seem to be bad; the temperature was 37.8 C. (100 F.); the pulse rate, 104. His abdomen was greatly distended and painful throughout. There was an absolute arrest of feces and even of gas. On account of the sudden onset of these peritoneal symptoms, it was thought that he had acute appendicitis with general peritonitis. Operation was performed seven and a half hours after the beginning of the symptoms.

A right iliac laparotomy was performed. On opening the abdomen, a rather large quantity of grayish fluid mixed with fragments of feces was discharged. However, nothing was found at the ileocecal angle or at the level of the appendix. A small amount of fecal material was found in the true pelvis. The iliac incision was then lengthened downward and inward, and the epigastric artery was ligated. The true pelvis could then be easily explored. It was literally filled with an enormous quantity of hard and pasty feces. After cleaning out the pelvis, a perforation the size of a 50 centime piece was found on the anterior surface of the sigmoid. The edges were slightly indurated for a short distance, and beyond the induration the mucosa of the colon was apparently normal. The edges of the perforation were resected, and the loss of substance was sutured in two layers. Although the peritoneum and the intestine did not appear to be inflamed, extensive drainage was inserted on account of the presence of such a large amount of feces in the abdomen.

During the following days, the patient seemed to support the operation well, there was no vomiting, his general condition was good, and he passed gas spontaneously. However, there was abundant suppuration from the abdomen. It was later learned that on June 16, this man again had abdominal pains with profuse vomiting which became fecaloid, and he died. It was believed that these symptoms were due to probable occlusion. Autopsy was not performed.

CASE 37 (Sieur,<sup>54</sup> 1920).—*Perforation of the Cecum.*

The patient was a man about 30 years of age. When the author saw him he had an acute abdominal attack which was so serious that it was thought advisable to send him to the hospital at once. The surgeon at the hospital did not believe that he would be able to operate and the patient died three days later. At autopsy, a perforation of the cecum was found. It was the size of a 50 centime piece.

53. Gregoire: Bull. et mêm. Soc. de chir. de Paris 46:420, 1920.

54. Sieur: Bull. et mêm. Soc. de chir. de Paris 46:421, 1920.

middle of the tumor proved to be an area about the size of a 2 mark piece covered with a fibrin deposit. On bimanual palpation, from the lumen of the intestine through an invagination in the wall of the cecum, this area was found to be a crater-shaped, rather long oval, sharp-edged ulcer, the inner and outer finger tips being separated from each other by a thin layer. The appendix did not show any pathologic change.

An appendectomy was performed. The pathologic part of the wall of the cecum was invaginated and buried in two stages by serosa sutures so that normal serous surfaces came together. Suture of the wall of the abdomen was done in two stages, without drainage. On April 16, the wound healed by first intention. Bowel movements were obtained only after enema. The patient's condition was good. In the histologic specimen of the appendix (serial sections), no pathologic changes were noted, particularly no tuberculosis. On April 25, the patient was up. Enemas were still necessary for bowel movements. Repeated examination of the stools for tuberculosis bacillus were negative. On May 11, a stool was passed after a purgative without any symptoms. The patient weighed 129 pounds (58.5 Kg.). She was discharged from the hospital cured.

CASE 41 (Ecot and Richard,<sup>23</sup> 1922).—*Perforation of a Simple Ulcer of the Ascending Colon.*

This recent observation on a perforation of a simple ulcer of the ascending colon, seen by the authors in the Service of Professor Pieree Duval, is of particular interest from the clinical point of view (syndrome of occlusion) as well as the anatomic point of view, the only one here considered. The specimen was removed in the course of the operation and showed a rounded, punched-out perforation of from 6 to 8 mm., with thickened margins, situated on the antero-external aspect of the ascending colon, 10 cm. above the ileal opening. The perforation permitted the escape of fluid material and gas; the patient at the time was suffering from perforation peritonitis. Excision of the ulcer, suture of the colonic wound and drainage were followed by recovery. Direct polymorphonuclear infiltration around the glands was visible at one extremity of the specimen. Embryonic infiltration was noted, especially abundant at the level of the muscular mucosa. Diffuse sclerosis, separating the fibers of the muscular mucosa layer, and perivascular sclerosis were also present, but no endarteritis. The capillaries were dilated and there was diffuse hemorrhagic infiltration. The serosa was slightly thickened. Accordingly, the condition was evidently long-standing mild sclerosis of the colon, apparently simple, as specific lesions of syphilis, tuberculosis or cancer, were not demonstrable at any point. The course of the disease became complicated in the following days by intestinal obstruction. An artificial left iliac anus was made.

CASE 42 (Dickinson,<sup>2</sup> 1922).—*Perforating Ulcers of the Cecum.*

A man, operated on, April 3, 1895, had had acute right inguinal pain and tenderness. There was no tumor. The rectal temperature was 101 F. The condition was diagnosed as appendicitis. A right rectus incision was made. The appendix was normal. The cecum was enormously distended, with three points of impending perforation 6 cm. in diameter. The peritoneum was reduplicated over these. Necropsy, five days later, revealed that the points of suturing held, but there were six new perforations in the cecum. These ulcerations were punctate, round, sharp margins, not necrotic.

CASE 43 (Idem).—A man, aged 22, operated on, Dec. 4, 1916, had suffered for a number of years with gassy dyspepsia, sour brash and delayed digestion, with relief on vomiting and never any pain. There was some discomfort in the

tine, but it was no more inflamed than the intestine and there was no perforation. A small round hole was found in the sigmoid from about 3 to 5 mm. in diameter, and about 12 cm. above Douglas' culdesac. The edges were infiltrated, and its appearance was that of a perforated ulcer of the stomach. The edges were excised, and a small wound in the intestine was closed. Drainage was established and the abdomen was partially closed.

The patient went into collapse on September 18. His pulse was scarcely palpable, and in spite of stimulants, he died in the evening.

Autopsy revealed normal thoracic organs. The stomach and the small and large intestines were opened. No inflammation of the mucosa or ulcer was found. The mucosa near the small intestinal wound in the colon was normal. Microscopic examination of the edge of the ulcer showed an infiltration of white cells. There was no evidence of tuberculosis.

CASE 40 (Levy,<sup>57</sup> 1921).—*Simple Ulcer of the Colon.*

E. F., a servant girl, entered the hospital on April 9, 1920. There was no history of tuberculosis in the family. She always had enjoyed good health until three years before, when she began having "stomach pain" lasting from one to two hours, which was so slight that she paid little attention to it. In September, 1919, she was treated for the first time in a hospital for pain that came on suddenly in the right side of the abdomen. She was discharged in ten days. She was admitted to the hospital again in January, 1920, for the same symptoms. Since that time she has frequently suffered from constipation and had to take purgatives. Three days before her present illness, she complained of dull pain over her whole abdomen which decreased a little after the passage of gas and a single stool, but the day before admission increased and became localized in the right side of the abdomen and from that time on was continuous. She did not suffer from vomiting. A hard stool was passed spontaneously in the night with severe pain. After that, the pain decreased considerably, but began again after about three hours.

Examination on admission, on April 9, 1920, revealed a large, strong girl in an excellent condition of nutrition. The left half of the abdomen was soft, without rigidity and without pain, and was compressible. On the right, a little inward from McBurney's point a rather long, oval, moderately hard tumor the size of a small hen's egg could be felt; it was movable and sensitive, particularly in the central part. There was no abdominal rigidity on the left and a trace on the right. Gynecologic examination revealed the uterus retroflexed, and no swelling of the adnexa.

The symptoms seemed to suggest appendicitis, though the symptoms on palpation left serious doubt of the diagnosis. The movable tumor inward from McBurney's point did not fit into the picture of appendicitis, in which the tumor, if there is any, is generally fixed firmly in the hollow of the sacrum. But operation seemed to be indicated.

Operation (Prof. Alsberg) was performed under general anesthesia. When the abdominal cavity was opened, turbid-serous fluid gushed out. A hard tumor could be felt on the wall opposite the ileocecal valve when the cecum was pulled out; it was about 3 by 6 cm. in size, long, hard, smooth and a little indented in the middle. Its red color was distinctly different from the velvet-red of peritonitis and showed dilatation and branching of the vessels. The inflammation of the

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57. Levy, Alfred: Simple Ulcer of the Colon, *Dtsche. Zeitschr. f. Chir.* 105: 356, 1921.

CASE 47 (Chalier and Mallet-Guy,<sup>59</sup> 1923).—*Simple Ulcer of the Ascending Colon.*

A man, aged 50, was admitted to the hospital on Oct. 3, 1921, with evidence of active pulmonary tuberculosis. Nothing else abnormal was found, and there was nothing to indicate any disorder of the digestive tract. This condition persisted without any marked change up to Jan. 23, 1922, with a temperature ranging between 99.6 and 101.1 F. On this date, diarrhea occurred without any previous colic and there was an intestinal hemorrhage. There were four stools of red blood without clots amounting to about 1 liter. At the same time his temperature went down to 98.9 F. and the patient became pale and enemic. He complained of vertigo and marked asthenia. The hemorrhage was relieved by rest, diet, applications of ice to the abdomen, by the administration of small, very hot enemas and the administration of calcium chloride and epinephrine. Several days later, when all danger seemed to be over, a careful and complete examination of the patient was made to determine the cause and location of the hemorrhage.

The respiratory symptoms were not changed. Rectal examination was negative. No abdominal tumor could be palpated, but the spleen was increased in size and extended about 2 inches beyond the costal border. In addition, there was dulness in the flanks which moved with a change in position and showed the presence of a slight degree of ascites. The intestinal hemorrhage was not repeated, and one and a half months before death he began to complain of pains in the umbilical region. He had a permanent burning sensation which was better after taking food. Three hours later there would be a marked increase of the pain. At this time the pains would be sharp, radiating to the left shoulder and persisting for two or three hours. They never terminated in vomiting, but were relieved by evacuation of the bowels. Diarrhea generally occurred. There were five or six stools daily, sometimes preceded by slight colic. His appetite was fair. Palpation was painful in the right iliac fossa. It was even more painful in the epigastric region just below the xyphoid and no tumor could be felt. His general condition became worse and it was not believed advisable to cause him to undergo the fatigue of a x-ray examination. Being confined to bed with his diet restricted, he rapidly became cachectic and he died on April 8, 1922.

At autopsy, the lungs showed evidence of tuberculosis. The right suprarenal capsule, to a large extent, showed caseation. The left suprarenal was normal. On the ascending colon about 5 cm. above the ileocecal valve, there was found on the antero-external surface an ulceration arranged transversely, perpendicular to the axis of the colon. This ulceration was of linear form about 1 cm. long and from 1 to 2 mm. wide. The edges of the ulcer were slightly elevated and were dark. The base of the ulcer appeared to reach the subserosa. There was no peritoneal reaction at this level. On examining the serosa, a small vessel could be seen by transparency. It was in a direction perpendicular to the axis, and a part of its course was exactly in relation to the base of the ulcer. This vessel was obliterated at a point in its course which corresponded to the center of the ulcer; it was undoubtedly this vessel which gave rise to the intestinal hemorrhage. The entire mucosa of the ascending colon was pink, while this coloration was absent in the rest of the intestine. The mucosa of the large intestine presented many folds without any appreciable lesions. No ulcer or other lesion was found on the small intestine, duodenum or stomach.

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59. Chalier, J., and Mallet-Guy: Simple Ulcer of the Ascending Colon. *Arch. d. mal. de l'appar. digest.* 13:521 (June) 1923.

appendicular region. The condition was diagnosed as chronic appendicitis or cholecystitis. The gallbladder was opened, disclosing dark bile, thickened with mucus, but no calculi. Drainage was instituted. The remainder of the abdomen was apparently normal on palpation and exploration, with the exception of the appendicular region. A second opening was made. The appendix was clubbed, fibrous, and excised through the tip of the cecum. On manipulation of the cecum to explore adhesions, a ligature in the cecal incision pulled off, with discharge of a substance resembling a dysenteric stool. The stoma was religated with linen thread. Necropsy, on the fourth day, revealed the ligature on the appendix stump in place. There was a ragged perforation of the cecum the size of a 5 cent piece opposite the ileocecal junction.

CASE 44 (Idem).—A man, aged 56, operated on, July 21, 1921, a clerk of good habits, experienced abdominal trouble three weeks before, starting with severe pain at the umbilicus, and green, watery vomitus. This recurred with intermissions. During the second week of the present illness, the pain shifted to the right lower quadrant. Vomiting continued, the vomitus becoming brown. The patient had been given considerable bismuth. Roentgenograms were taken. There had been no action of the bowels in ten days. On admission to the hospital, the patient presented marked pyrexia, coated tongue and reddened throat. Pain, rigidity and tenderness were noted at the cecal region, particularly on deep pressure. The heart sounds were distinctly heard at the pubes. As some type of appendicitis was suspected, an incision was made through the right rectus sheath. When the peritoneal cavity was opened, a puff of gas was heard. The peritoneum and viscera were markedly injected, and purplish red. The appendix was normal. The cecum was agglutinated to the lateral wall. When it was lifted up, liquid feces exuded from several small openings in the ulcerated areas, about opposite the ileocecal junction. These points of ulceration were about 6 cm. in diameter. In view of previous experiences, the cecum was stitched to the abdominal peritoneum and incised freely. Bismuth feces were removed. Convalescence was protracted, and during it the patient developed exfoliated stomatitis, associated with which was complete anorexia and an intolerance by the stomach even for water, except in small quantities.

CASE 45 (Bowen,<sup>4</sup> 1922).—*Perforation of the Large Bowel.*

A woman of middle age with a negative gastric history was taken suddenly with severe abdominal pain, nausea and vomiting. Eight hours later, the abdominal wall was rigid and the signs indicated a perforation. Operation revealed fecal material in the abdomen, and a perforation of the sigmoid. The walls of the colon were described as rotten, and they only tore on attempts to suture. The woman died, but autopsy was not permitted. The author was unable to get a clear idea of the abdominal condition, but thinks the perforation probably resulted from thrombosis. Evidence in favor of a stercoral ulcer or foreign body was scanty.

CASE 46 (Idem).—A woman, aged 27, who had been suffering from gastric ulcer, developed severe pain all over the abdomen, with a definite right sided rigidity, and maximum tenderness just above and internal to the anterior superior spine. Operation revealed an acute catarrhal appendicitis, with a perforation in the cecum, near the ileocecal valve. There was no free fluid in the abdomen, the perforation having been closed by some valve action. As no constipation had been present, a stercoral ulcer can be ruled out.

58. Bowen, W. H.: Five Cases of Perforation of the Large Bowel, *Guy's Hosp. Rep.* 72:441 (Oct.) 1922.

ulcer was caused by a fecolith. The perforation orifice was found to contain a hard fecal mass. The symptoms observed during life, at the time of perforation, in the form of profuse hemorrhage from the anus and sudden onset of pain, were explained by the (microscopically) distended and congested vessels, which extended almost to the intestinal lumen. In spite of her advanced age, the patient had been in good condition up to a few months before her admission to the hospital on account of general weakness. As she suffered from chronic constipation, cascara was regularly administered. Her condition some months later was entirely satisfactory, when she was suddenly attacked by severe abdominal pains. The abdomen was painful on palpation, with some muscular defense. On three occasions, the patient passed a few small scybala with about 75 and 100 cc., respectively, of fluid, unchanged blood, without mucus. The results of the rectal examination were negative. At night, her hands became cold and the heart sounds became weaker; the pulse rate was 120 and weak. In the course of the next day, the temperature rose, the condition became aggravated, the pulse rate increased to 160, was weak and small, and at the end of the second day after the onset of the symptoms of perforation, the patient died. The autopsy explained all symptoms, indicating that the microscopically greatly congested vessels, reaching nearly to the intestinal lumen, were responsible for the profuse hemorrhages from the anus at the time of the perforation, with simultaneous onset of severe pains.

CASE 50 (Boss,<sup>21</sup> 1927).—*Perforating Ulcer of the Large Intestine.*

A man, aged 38, entered hospital on Aug. 8, 1921. Eleven years before he had had gastro-intestinal catarrh while in Arabia which lasted eleven days; ten years before he had had malaria in India. There were no further intestinal disorders. On August 7, the afternoon previous to his admission, while in perfect health, he had had sudden, violent, convulsive pain in the umbilical region and vomiting. On August 8, the day of admission, he passed a black stool. Vomiting and pain persisted in spite of the administration of narcotics. Peritonitis was suspected, and he was sent to the surgical ward of the hospital. On admission, physical examination showed him to be a robust man, in fair condition of nutrition, healthy appearance of skin and face. The blood picture revealed 11,200 leukocytes with 90 per cent polymorphonuclears. The temperature was 102 F.; pulse rate, 110, regular and full. The results of the physical examination were negative except that in the abdomen, the scaphoid was indrawn; there was intensive resistance, and the greatest pressure pain in the region between the navel and the symphysis. The urine was normal. A diagnosis of peritonitis was made, and operation was immediately performed.

A median laparotomy was performed. The small intestines were reddened. There was some pus deep in the pelvis. It was more abundant in the median line than in the region of the appendix. The appendix was free and was found not to be responsible for the peritonitis. The intestines in the pelvis were covered with fibrin. In the lower portion of the sigmoid, there was a perforated ulcer the size of a bean from which feces were discharged. The tissue in the vicinity of the ulcer was not infiltrated but reddened. The ulcer was closed by five longitudinal catgut sutures and two rows of catgut sutures. To relieve the strain on the sutures, a broad colostomy was made in the descending colon, three handbreadths above the suture line.

Two days after operation, there was a large stool from the fecal fistula. The patient made an uneventful convalescence and was discharged as well on December 15. Four weeks after operation sigmoidoscopy revealed a normal condition of the mucosa for 22 cm. The ulcer had disappeared.

Histologic examination revealed a simple ulcer of the colon without any tuberculous or neoplastic formation. The edges of the ulcer were raised. The ulcer had extended through the muscularis mucosa and had deeply penetrated the muscular layer. This progression was accompanied by a marked lymphocytic reaction. The vessels of the subserosa were obliterated. The right suprarenal was cascated, but there were some traces of glandular tissue. Giant cells were found. The section included a sympathetic ganglion, which was normal.

CASE 48 (Mintz,<sup>60</sup> 1923).—*Simple Ulcer of the Colon.*

A girl, aged 18, took sick with vomiting and abdominal pains, evacuation of fifteen nematodes took place five days after castor oil had been given. Within the next eleven days, intermittent attacks of colic and constipation occurred. On the sixteenth day, the attending physician established evidence of a mobile tumor in the ileocecal region and prescribed oleum chenopodii, whereupon another ascaris was evacuated. On the seventeenth day, during examination in my department, an extremely mobile tumor was found below the umbilicus. The diagnosis of chronic invagination was confirmed by the x-ray examination. Seven hours after ingestion of the contrast meal, the lower ileum and also part of the ascending colon were filled, and the invagination of the ileum loop could be directly seen on the plate. Stools that resembled the fecal matter of sheep were passed on the same day. On the evening prior to operation (twentieth day of the disease), the colicky pains, which had been constant and slight, became more severe. The tumor became enlarged to a cylinder which disappears obliquely upward to the left underneath the costal arch. Later on, vomiting set in. Immediate surgical intervention was advised. The ileum, cecum and ascending colon were invaginated into the transverse colon. Disinvagination of the edematous intestinal parts was performed without difficulty. In the cecum, a hard indentation of the wall, opposite the orifice of the ileum was noticeable. This was the size of a 1 mark piece. The serosa over it was thickened and flaming red—in short, the picture was presented that one sees on the serosa over peptic ulcers. Typical ileocecal resection was performed. The patient had an uneventful postoperative course.

The cecal wall as a whole was unchanged. The indentation appeared to have been due to the inflexibility of the diseased place in contrast to the distended, healthy adjacent parts. On the mucous membrane, there was a sharply defined ulcerated surface of the size of a 1 mark piece which corresponded to the indentation. This surface was of brownish red and contrasted markedly from the completely healthy appearing adjacent mucous membrane. A similar ulcer the size of a pea was situated 1 cm. away from it, at the same level.

Microscopic examination revealed the serosa considerably thickened, with newly formed dilated vessels. The larger ulcer showed a sharp demarcation from the surrounding area, loss of mucous membrane, small celled infiltration and scattered necrotic foci, which are also found in the muscularis. On the little ulcer, similar conditions were found which did not penetrate so deeply. Thrombosing endarteritis could not be demonstrated.

CASE 49 (Broere,<sup>61</sup> 1923).—*Decubitus Ulcer of the Colon.*

This contribution comes from the Pathologico-Anatomical Laboratory of the Wilhelmina Institute in Amsterdam, and concerns the autopsy observations in the case of an old woman 80 years of age. An ulcer was found at the transition of the rectum into the sigmoid flexure of the colon. Rupture of a so-called decubitus

60. Broere, W. J.: Decubitus Ulcer of the Colon, Nederl. Tijdschr. v. Geneesk. 67:2274, 1923.



# "STREAM LINE" PHENOMENA IN THE PORTAL VEIN AND THE SELECTIVE DISTRIBUTION OF PORTAL BLOOD IN THE LIVER \*

GLOVER H. COPHER, M.D.

AND

BRUCE M. DICK, M.B., F.R.C.S. (Edin.)  
ST. LOUIS

There have been a few experimental and clinical studies that have suggested the possible occurrence of a selective distribution of portal blood in the liver and the presence of independent currents of blood in the portal vein. Final proof of the presence of these currents has not been established, and the selective distribution of portal blood in the liver has been held in doubt. The possible existence of segregated streams of blood in the portal vein and their subsequent distribution to definite parts of the liver is of interest and should be of considerable practical significance in the study of the physiology and pathology of the liver. The evidence in favor of the existence of these phenomena has not generally been known or seemingly accepted.

In 1901, Sérégé<sup>1</sup> injected india ink into the splenic vein of the dog and found particles only in the left lobe of the liver; when the ink was injected into a tributary of the large mesenteric vein, particles were found only in the right lobe. These experimental observations were confirmed by Glenard.<sup>2</sup> Bauer<sup>3</sup> and several other workers repeated the experiments, but they were unable to distinguish any difference in the distribution of the india ink, and therefore denied the existence of a dual portal current. In 1907, Loeb<sup>4</sup> found that the iodine content of the right lobe of the liver of rabbits was constantly greater than that of the left one hour after subcutaneous injection of potassium iodide. This observation was confirmed by Wells<sup>5</sup> and Hedenburg.

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\* From the Department of Surgery, Washington University School of Medicine, and Barnes Hospital, St. Louis.

1. Sérégé, H.: Contribution à l'étude de la circulation du sang porte dans le foie et des localisations lobaires hépatiques, *J. de méd. de Bordeaux* **31**:271, 291 and 312, 1901.

2. Glenard, F.: Note sur les localisations lobaires hépatiques, *Bull. et mém. Soc. méd. de hôp. de Paris* **18**:386, 1901.

3. Bauer, A., and Brissant, E.: L'indépendance des lobes du foie est hypothèse, *J. de l'anat. et de la physiol.* **45**:1, 1909.

4. Loeb, O.: Die Jodverteilung nach Einfuhr verschiedener Jodverbindungen, *Arch. f. exper. Path. u. Pharmacol.* **56**:321, 1907.

5. Wells, H. G., and Hedenburg, O. F.: Studies in the Biochemistry and Chemiotherapy of Tuberculosis: The Permeability of Tubercles for Iodin Compounds and Proteins, *J. Infect. Dis.* **11**:349, 1912.

Roentgen-ray examination of the intestine after a barium meal and a barium enema showed that in passage from the descending portion of the large intestine into the sigmoid flexure, a constriction occurred, lasting several hours, at a point which corresponded to the location of the sutured ulcer. The following history was obtained from the patient some time after his operation: Six months before the perforation, the patient had had an accident while carrying a heavy load. He had slipped and fallen, injuring his back. From that time on he had had considerable abdominal pain when lifting heavy weights.

Cases 51, 52 and 53 are my cases 1, 2 and 3 which have been reported earlier in this paper.

and be maintained in the portal vein, we made a careful study of the portal system and its tributaries and also of the mode of termination of the portal vein in the liver.

#### THE ANATOMY OF THE PORTAL VEIN IN THE DOG

##### *Mode of Termination of the Portal Vein at the Hilum of the Liver.*

—At the hilum of the liver, the portal vein divides into two main branches; the division takes place at an angle of about 170 degrees. The right branch of the portal vein is smaller and has a much shorter course than the left branch.

The right branch of the portal vein is distributed entirely to the two lobes of the liver which lie most laterally. After a short course outside the liver, the vessel divides into two or four branches, and one, or a pair of these, passes into each of the two right outer lobes.

The left branch of the portal vein traverses the hilum of the liver for a distance of about 5 cm.; in its course it gives off three branches which come off at right angles to it and pass directly to the three intermediate lobes of the liver; some of these branches may be paired. The main vessel ends by dividing in a radiate manner into five branches; each of the two large left lobes receives two branches, while the fifth branch passes into the small lobule of liver which is situated immediately to the left of the gallbladder; this lobule also receives a branch from the main left trunk (figs. 1 and 2).

It will be observed that strict *anatomic* bilaterality of the portal vein does not obtain in the dog's liver as it does in that of the human subject. In the dog, the left branch of the portal vein supplies two thirds of the whole organ; the right branch of the portal vein delivers blood only to the two outer right lobes of the liver.

*Intrahepatic Course of the Portal Vein.*—The intrahepatic course of the portal vein was studied in specimens in which iodized oil (40 per cent) had been injected into one of the tributaries of the portal vein in a living dog. Roentgenograms of the excised livers were taken, and an exact outlining of the venous channels was obtained (fig. 2).

It was observed that the main vein of each lobe splits up in an arborescent fashion, and that there is no anastomosis between the larger branches. The larger branches of the portal vein and their smaller ramifications are clearly displayed in figure 2. When livers from human beings had been injected with iodized oil 40 per cent a similar distribution of the portal vessels was demonstrated; furthermore, the strictly sectorlike distribution of the large portal branches suggest that the human liver may be regarded as a multilobar organ resembling closely the dog's seven lobed liver.

In 1914, Bartlett,<sup>6</sup> Corper and Long studied the problem. Olive oil emulsified in blood serum was injected into different parts of the portal system of the dog. After counting the number of fat emboli in microscopic sections of different parts of the liver, they concluded that a dual portal current exists in the dog's portal vein; and that blood from the stomach, spleen, duodenum, first portion of the jejunum and rectum flowed mainly to the left lobe of the liver, while blood from the lower portion of the jejunum, the ileum and the first portion of the large intestine flowed mainly to the right lobe.

More recently, McIndoe<sup>7</sup> and Counseller made anatomic studies of the liver in man by means of the celloidin-corrosion method; these studies indicate an anatomic division of the liver into two separate units. These workers have demonstrated that the area of distribution of the right and left branches of the portal vein in the human liver is sharply divided along a line from the fossa for the gallbladder to the entrance of the hepatic veins into the inferior vena cava, and that the only communication between the two vessels is through intercellular sinusoids. The same line of demarcation separates the field of supply of the branches of the right and left hepatic artery and also the branches of the two hepatic ducts. The line of lobar separation, as determined by the celloidin method, corresponds to the recognized embryologic boundary between the right and left lobes of the liver.

In the present investigation, we made a study of the blood currents in the portal vein itself, and observed the subsequent distribution of the blood in the lobes of the liver. Dyes were injected into different radicles of the portal vein of the dog, and their ultimate localization in the liver was observed. The advantages of this method are that the injected material can immediately be visualized in the part of the liver to which it has been conveyed, and that the dye-stained blood can be seen in the portal vein when the vessel is submitted to powerful transillumination. The method overcomes the objections to the use of particulate matter for intravenous injections.

At the outset of this experimental study, emulsified iodized oils were introduced into various parts of the portal circulation, and roentgenograms of the liver were obtained. An unequal distribution of the iodized oil was often noted, but the site in the liver in which the oil localized itself was inconstant.

As we believed anatomic considerations would be of importance in determining the way in which a system of stream-lines might arise

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6. Bartlett, Corper and Long: The Independence of the Lobes of the Liver, *Am. J. Physiol.* **35**:36, 1914.

7. McIndoe, A. H., and Counseller, V. S.: Bilaterality of the Liver, *Arch. Surg.* **15**:589 (Oct.) 1927.

portal vein; it joins the mesenteric vein at an angle of about 45 degrees. About 2 cm. from its termination, it receives a branch from the posterior part of the stomach and lesser curvature.

**Large Mesenteric Vein<sup>8</sup>:** The large mesenteric vein is larger than the splenic vein; it drains blood from the lower part of the duodenum and the whole of the small intestine. Near its termination it has a linear course, and the portal vein appears to be a direct continuation of it.

The small mesenteric vein<sup>8</sup> enters the large mesenteric vein at an angle of about 5 degrees, less than 1 cm. below the point of union

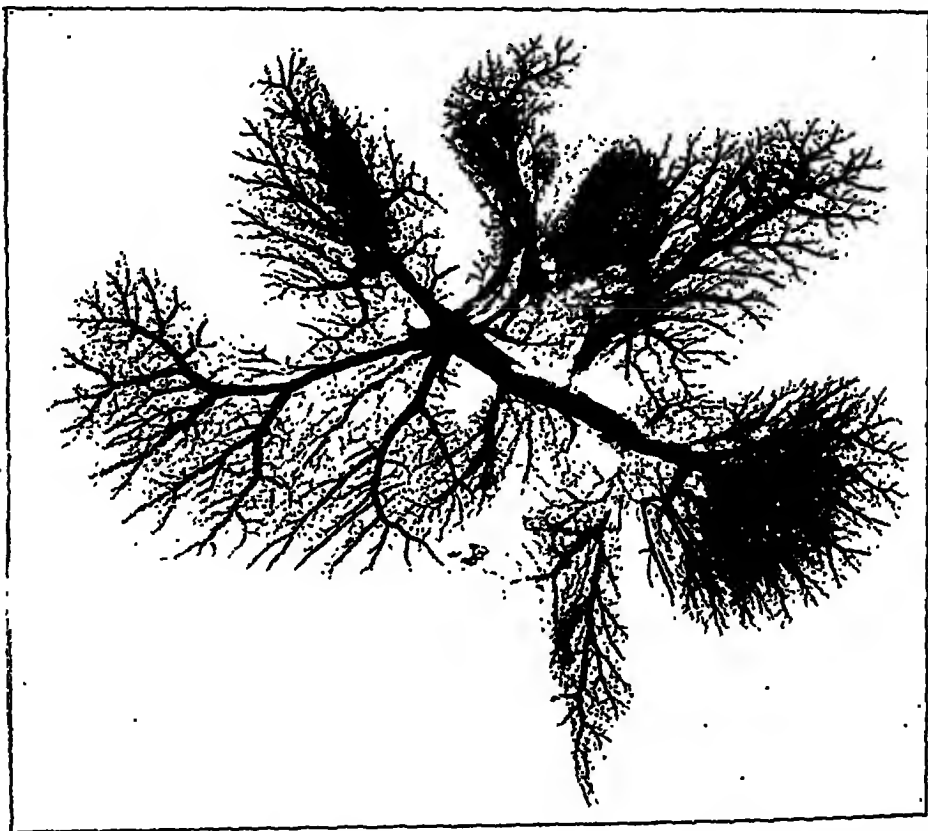


Fig. 2.—Dog's liver after intraportal injection of iodized oil. Note the arborescent character of the large portal veins and the absence of large intralobar anastomoses.

of the splenic and large mesenteric trunks. The small mesenteric vein drains blood from the whole of the colon; it has two main branches. The right branch comes from the cecum and the first part of the colon; the larger left branch collects blood from the distal part of the colon and rectum. The two branches unite into a short common stem that

8. In works on anatomy of the dog the mesenteric veins are called large and small. The large vein corresponds to the superior vein of the human subject; the small vein corresponds to the inferior mesenteric vein.

*The Anatomy of the Portal Vein and of Its Tributaries.*—In the dog, the average length of the portal vein is 8 cm. It begins dorsal to the neck of the pancreas by the union of the splenic and large mesenteric veins. The vessel runs in a cephalad direction, dorsal to the superior part of the duodenum, between the two layers of the lesser omentum to the right end of the porta of the liver, where it divides into a right and a left branch.

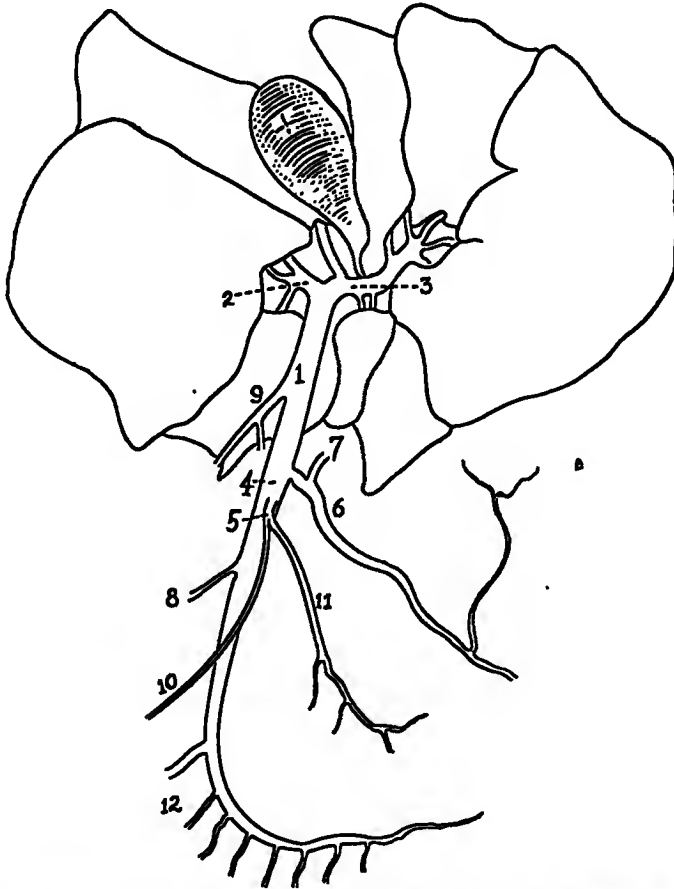


Fig. 1.—Diagram of the portal system of the dog showing the main tributaries and the mode of termination of the vessels at the hilum of the liver. 1 indicates the portal vein; 2 and 3, the right and the left branch of the portal vein, respectively; 4, the main mesenteric vein; 5, the small mesenteric vein; 6, the splenic vein; 7, the gastric branch of the splenic vein; 8, the lower pancreaticoduodenal vein; 9, the upper pancreaticoduodenal vein; 10 and 11, the right and the left branches of the small mesenteric vein and 12, the enteric branches of the large mesenteric vein.

**Tributaries:** The chief tributaries are the splenic, the large mesenteric and the upper pancreaticoduodenal vein.

**Splenic Vein:** The splenic vein runs to the right from the hilum of the spleen and ends by joining the large mesenteric vein to form the

lobe of the liver constantly received a portion of the dye. The remainder of the right side of the liver retained its normal chestnut color, and the dye did not register itself in any part of it.

**Stomach:** The injection was made into a small vein on the lesser curvature. The whole of the left half of the liver was uniformly stained by the dye. The line of separation between the right and left lobes was sharply demarcated and thrown into striking contrast by the unilateral staining of the liver. No trace of dye was recognized in the right side (fig. 3).

**Pancreas and Upper Part of Duodenum:** An injection was made into the superior pancreaticoduodenal vein. The dye was constantly carried to the right side of the liver; the two lobes on the extreme right of the liver were deeply stained. A small amount was deposited in the right border of that lobe which adjoins the two more lateral lobes (fig. 4).

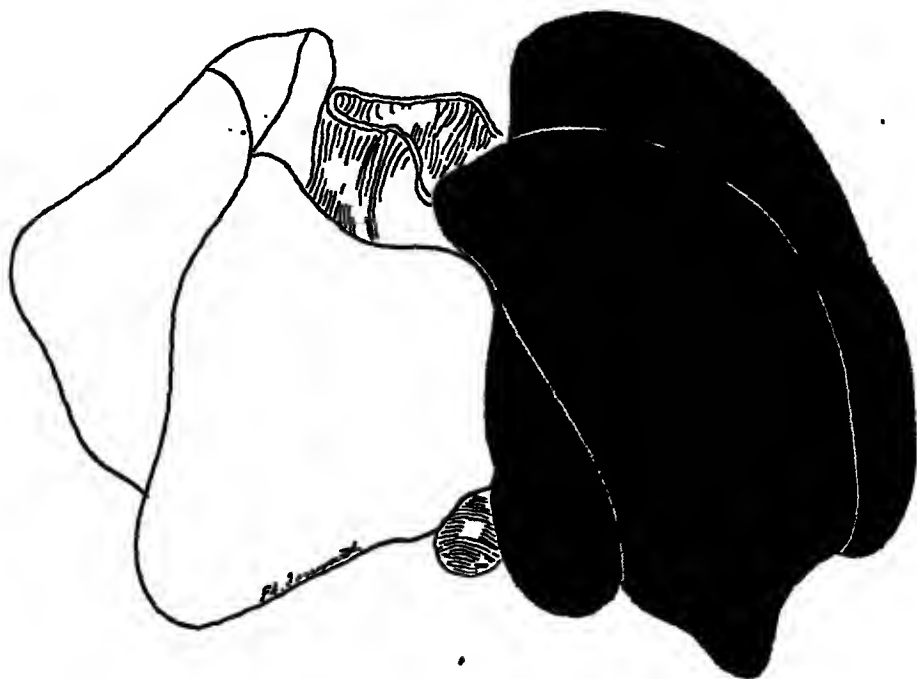


Fig. 3.—Dog's liver drawn from a specimen to illustrate the distribution of trypan blue after the injection into a gastric branch of the splenic vein. The black area denotes the part of the liver that was stained by the dye.

An injection was made also into the inferior pancreaticoduodenal vein. The dye was carried mainly to the right half of the liver, although a certain amount reached the left side. The lobe which lay immediately to the right of the gallbladder always showed deeper staining than any other part of the liver.

**Jejunum:** Dye was injected into a mesenteric vein at the highest part of the jejunum. The bulk of the dye registered itself in the two extreme right lobes of the liver. Scattered spots of coloration were seen occasionally in the left half of the liver but never more than a few (fig. 5).

**Cecum and Appendix:** A small vein at the root of the meso-appendix was selected for injection. The dye was transported to all parts of the liver. The large outer left lobe of the liver generally showed a greater deposition of dye than other parts, and was stained more deeply than the rest of the liver. In some dogs, the right half of the liver showed a greater amount of dye than the left.

enters the left side of the large mesenteric vein a little toward its ventral aspect. In some dogs, the right and left branches of the small mesenteric vein do not unite to form a common vessel, but enter the large mesenteric vein separately at the same level. In such instances, the branch from the left portion of the colon enters on the left side of the large mesenteric vein, and the right terminates about the center of the ventral aspect of the main mesenteric trunk.

**Pancreaticoduodenal Veins:** There are two of these vessels. The upper pancreaticoduodenal vein drains the head of the pancreas and the first part of the duodenum and also receives a small tributary from the pyloric area. The vein ends by joining the portal vein on its right side, about 2 cm. below the hilum of the liver. The lower pancreaticoduodenal vein derives blood from part of the head of the pancreas and the distal part of the duodenum; it ends by joining the right side of the large mesenteric vein about 5 cm. from the termination of this vessel.

#### EXPERIMENTAL STUDY OF THE DISTRIBUTION OF THE PORTAL BLOOD CURRENT IN THE LIVER

*Method.*—Trypan blue, dissolved in blood serum, was employed as the coloring agent for the study of the portal blood current. One gram of trypan blue crystals was dissolved in 15 cc. of blood serum; 3 cc. of this solution was the amount generally given at each intravenous injection of the portal radicles; the quantity was varied slightly according to the size of the dogs employed. The advantages of the dye are its lightness and solubility, and the parts of the liver to which it is conveyed by the blood stream are immediately colored. The staining of the liver persists for some time, and formaldehyde preservation of the specimens does not obliterate the coloring.

The dogs were anesthetized with ether, the abdomen opened, and the various portal tributaries injected with trypan blue solution; the animals were killed with ether soon after the injections, and the liver was removed for examination. Injections were, as a rule, made into the smallest veins that could be easily entered by a hypodermic needle; care was taken not to disturb the normal position of the viscera when the injections were being carried out. About thirty seconds was the average time taken to complete an intravenous injection, and only gentle pressure was employed. In some instances, the position of the animal on the operating table was altered in order to study the effect of posture. The experiments were repeated many times for each part of the portal vein that was under investigation. In all, about 100 experiments were performed.

*Sites of Injection and Results.*—In the following descriptions, the liver is regarded as being divided into right and left halves by a line passing from the fossa for the gallbladder to the entrance of the hepatic veins into the inferior vena cava. It was noted that in the canine liver this division does not correspond to the anatomic distribution of the two main branches of the portal vein.

*Injection of Splenic Vein:* A venule at the lower end of the hilum was selected for injection. Almost the whole of the left lobe of the liver was colored by the dye. It was observed that a limited area of the upper part of the extreme right



*The Disappearance of the Dye from the Liver.*—In some instances, the behavior of the dye in the liver was observed before the animals were killed. It was noticed that when the dye had restricted itself to a particular portion of the liver there was only a slight tendency for diffusion to occur to a part beyond the initial site of localization. After from five to ten minutes, the dye commenced to disappear from that part of the liver in which it had first deposited itself. The liver as a whole assumed a slightly darker color throughout, but only to the same degree as the other organs of the body that, for a time, became tinted light blue when the dye reached the systemic circulation.

*The Effect of Large Injections of Dye.*—When the trypan blue was injected in a large quantity the liver was colored throughout, but the staining was not equal in all parts; for example, if a large volume of dye was injected into the splenic vein the whole liver became blue, but the staining was always more pronounced in the left side.

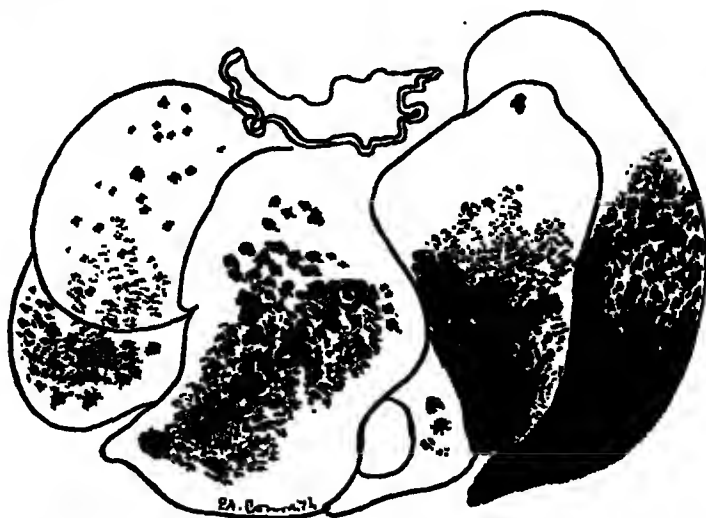


Fig. 6.—Distribution of dye after injection of a vein in the mesentery of the lower part of the colon.

#### VISUALIZATION OF THE CURRENTS WITHIN THE PORTAL VEIN

*Method.*—The peritoneum was denuded from the surface of the portal vein and its larger tributaries near their termination. The experiments were carried out in a darkened room. A Cameron curved abdominal light that transilluminated the interior of the vessels was placed immediately behind the portal vein. The moving blood current was evident at once, when the light was placed in situ. Small dogs were used in these experiments so that effective transillumination of the portal vein could be obtained more readily. Trypan blue dissolved in blood serum was introduced into different branches of the portal system, and the transilluminated portal vein was kept under observation while the injections were being made. The injections were made slowly and with great gentleness.

A striking demonstration of sharply defined intraportal currents was afforded by this method, and the extreme rapidity of blood flow in the portal vein was made evident.

*Sites of Injection and Results.*—*Splenic Vein.* The injection was made near the hilum of the spleen. The dye-stained blood was seen to enter the left side of the portal vein obliquely. The dark stream kept strictly toward the left side of the

**Descending Colon and Rectum:** The large vein in the mesentery of the left part of the colon was selected for injection. The dye was distributed throughout the liver. A greater amount of dye was evident in the left side, more especially in the large lobe on the extreme left side of the liver (fig. 6).

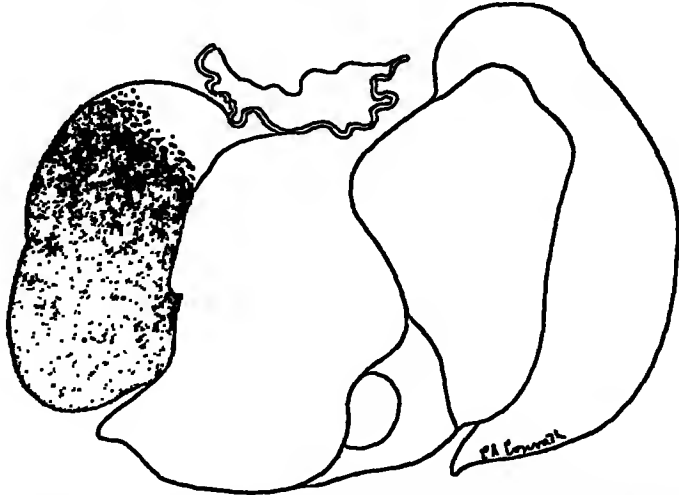


Fig. 4.—Distribution of dye after the injection of trypan blue into the upper pancreaticoduodenal vein of the dog. The darkly shaded area indicates the part of the liver to which the dye was carried.

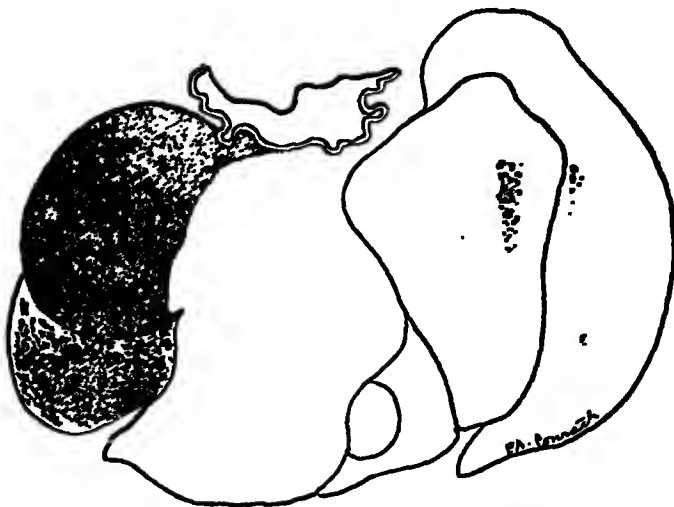


Fig. 5.—Distribution of dye after the injection of a mesenteric vein of the upper part of the jejunum of the dog.

**Large Mesenteric Vein:** The dye was injected at a point just distal to the entrance of the small mesenteric vein. The dye was deposited in the two lobes at the extreme right of the liver; a little was carried to the lobes of the left side.

**The Effect of Posture.**—Alteration of the position of the animal on the operating table, such as turning the trunk to one side or supporting the animal in the quadruped position while an injection was made, did not alter the character of the experimental observations.

It may be inferred from these facts that possibly blood that has been conveyed from the periphery of the portal system to a particular section of the liver is utilized in that specific area without contact with blood from other parts of the portal tree. It is of interest to note that, according to our experimental observations, the blood which is carried to the left lobe of the liver is drained principally from those abdominal organs that are not strictly engaged with the digestion or absorption of food, namely, the spleen, the stomach and the greater part of the colon; whereas, the blood collected from those parts of the alimentary tract where the products of digestion are absorbed is carried to the right side of the liver and, in the dog, often to a special and constant site in that lobe. For example, the blood from the upper pancreaticoduodenal veins is conveyed to the two lateral lobes of the right side of the liver.

In brief, it would seem from our evidence that there are areas in the liver which are especially supplied with blood from specific parts of the portal system, and that the blood from the different parts of the portal system does not become mixed in the liver nor, as we shall indicate, in the portal vein itself.

An explanation for the selective distribution of the portal blood in the liver is afforded by the visual demonstration of stream lines in the transilluminated portal vein after the injection of dyes. These currents serve to transport blood from the periphery of the portal system to the liver in such a manner that little or no intermingling of the individual blood streams occurs in the main portal channel. It would seem from our experiments that there are at least three main blood currents in the portal vein. These currents are, in our opinion, derived from three sources, namely, the splenic vein, the large mesenteric vein and its branches and the small mesenteric vein. In our observations, three sets of currents were initiated and maintained in the portal vein by these three large vessels.

Maintenance of individuality of different currents in the portal vein finds a counterpart in at least one other human circulatory system. In the fetal heart, blood from the superior and inferior vena cava does not mix freely in the right auricle. Likewise, the individual currents in the portal vein may be likened, in part, to the union of two rivers, for example, the Rhone and the River Avre, one clear and the other muddy, that retain their identity for a considerable distance after their union in a common stream-bed. This phenomenon of separate streams in a moving body of water is well known to hydraulic engineers and is usually discussed under the name of "stream lines." The anatomic disposition of the splenic, large mesenteric and small mesenteric veins would seem to be favorably adapted to the ejection of blood into the main portal channel in such a direction that the

portal vein and preserved a narrow, ribbon-like course throughout the portal vein up to the hilum of the liver. No mixing with the adjacent blood in the portal vein was observed, and a cleancut linear division between the narrow splenic and the broad mesenteric streams was seen throughout the length of the portal vein. The injection was continued for several minutes, and at no time was there any alteration in the character of the current.

**Injection of Jejunal Vein:** A vein in the mesentery of the upper part of the jejunum was selected for injection. The stream was narrow and was sharply demarcated. It maintained an undeviated course along the right wall, and no mixing with red blood was seen to occur as it traveled to the hilum of the liver.

**Small Mesenteric Vein:** The large vein in the mesentery of the descending colon was selected for injection. A thin linear current of blood was visualized in the center of the ventral aspect of the portal vein. The current preserved an absolutely undeviated course throughout the length of the portal vein, and diffusion into other parts of the vessels did not occur.

#### COMMENT

We have found by the injection of trypan blue into tributaries of the portal vein of dogs that, with few exceptions, the dye is transported in the portal blood stream to fairly constant and definite areas in the liver, and that the site varies according to the place at which the dye is introduced peripherally. In our experiments, we found that when trypan blue was injected into the veins of the stomach and spleen it was conveyed by the blood to the left half of the dog's liver almost entirely. Dye injected into the veins of the upper part of the duodenum, the head of the pancreas and the jejunum was carried to the right lateral lobes almost exclusively. When the veins of the colon were injected, the dye was distributed to all parts of the liver, but more particularly to the large lobe of the left side. In those instances, in which the two colonic veins did not unite in a common mesenteric trunk but had a separate termination in the large mesenteric vein, it was found that injection of the right vessel resulted in a more liberal distribution of the dye in the right side of the liver.

Trypan blue stains the parenchyma of the liver and the coloration remains for some time. Once the dye is carried to a particular region of the liver, the staining remains sharply circumscribed. The terminal character of the lobar divisions of the branches of the right and left portal vein and the absence of interlobar and intralobar venous anastomoses are responsible for the absence of visible diffusion to other parts of the liver. The temporary staining of the liver does not signify that the blood which conveyed the dye has itself remained confined in a demarcated area of the liver for so long a period, as the dye is almost immediately recognizable in the systemic circulation after intraportal injection; furthermore, the volume of flow of portal blood through the liver is rapid; in the dog, 60 cc. of blood per hundred grams of liver in a minute.

# THE RÔLE OF THE CIRCULATION IN THE HEALING OF FRACTURES

A REVIEW

WILTON H. ROBINSON, M.D.

PITTSBURGH

Normal Blood Supply of Bone.

Effect of a Fracture on the Adjacent Arterial Circulation.

Effect of Cutting the Veins and Lymphatics at the Site of Fracture.

Incompressibility of Muscle Tissue and the Effect of This on the Circulation of Blood to a Fracture Area.

Relation of the New Bone Trabeculae to Blood Vessels.

The Laying Down of Lime Salts.

Development of Fibrous Tissue.

Summary.

Conclusions.

In 1863, Hamilton<sup>1</sup> estimated the incidence of nonunion of fractures to be one in 500 cases. Scudder and Hey-Groves,<sup>2</sup> in 1927, placed it, respectively, at from 2 to 3 and from 3 to 5 per cent. If it is true, but this is doubtful, that there is a larger percentage of delayed unions and nonunion of fractures today than formerly, it may easily be accounted for by the greater traumatisms sustained today and by the more exacting standards under which the surgeon works, but whether it is true or not, the fact still remains that a better conception of all the vital processes concerned in bone repair will result in diminished morbidity.

In this article are presented some salient facts relative to the circulation and its possible relation to the repair of a fracture.

The repair of a fracture is by a group of interrelated processes by no means well understood. These processes are: (1) the establishment of the circulation in preparation for the definite construction of bone; (2) dissolution, partial or complete, of the old bone and the laying down of lime salts to form new bone, which, architecturally, is not the same as the old, and (3) rearrangement of the new bone to carry the particular stress to which that section of bone is subjected.<sup>3</sup> While these processes occur in the order given, they overlap so that two or even all may be going on at the same time. Throughout all processes of bone repair, the circulation is of primal importance, and by this is meant, not only the arterial circulation, but that of the veins and lymphatics, for without the elimination of the waste products, repair will be impossible.

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1. Hamilton, F. H.: *A Practical Treatise on Fractures and Dislocations*. Philadelphia, Blanchard and Lea, 1863, p. 61.

2. Bancroft, F. W., and Scudder, C. L.: *The Treatment of Fractures*, ed. 10. Philadelphia, W. B. Saunders Company, 1926, p. 949.

3. Koch, John C.: *The Laws of Bone Architecture*, *Am. J. Anat.* 21:177 (March) 1917.

individual streams could remain separate. These anatomic advantages are probably further aided by the known differences in the rate of flow in the veins, their relative tonicity and differences in viscosity of the blood they contain.

#### SUMMARY AND CONCLUSIONS

1. The distribution of the portal blood in the liver of the dog was determined by the injection of a dye.

2. Blood from the spleen, the stomach and a greater part of the colon goes to the left lobe of the liver; whereas blood from the duodenum, the head of the pancreas and the upper part of the jejunum goes mainly to the right lobe of the liver.

3. A satisfactory method of visualizing experimentally the individual currents of blood in the portal vein is presented.

4. There are at least three distinct and separate currents in the portal vein.

5. The anatomy of the portal vein and the intrahepatic distribution of its blood in the dog were studied and the results have been presented.

## EFFECT OF A FRACTURE ON THE ADJACENT ARTERIAL CIRCULATION

It may be accepted as axiomatic that repair of a fracture depends on the establishment of adequate channels of blood circulation to the injured area. Kolodny has shown by injected specimens<sup>8</sup> that following a fracture there is increase in the diameter and in the tortuosity of all the arterial vessels in the section of the limb adjacent to the fracture.

Coincident with the occurrence of a fracture of a long bone there is damage to the normal blood supply. The longitudinal vessels are torn or cut by the shearing action of fragments, and the periosteal vessels are torn where the periosteum is separated from the cortex of the bone by avulsion. Bleeding immediately occurs from the injured vessels. In due time, a clot is formed about the fragments; lineal projections of this clot extend into the lumen of the arterial vessels until they reach the nearest patent collateral, and thus thrombi are formed in the vertical trabecular spaces of the bone for a varying distance below and above the actual line of fracture.

The clot in the longitudinal bone channels, i.e., the thrombi and that between the fragments, must be spoken of separately. The former no doubt will resolve by the same processes as will a thrombus of soft parts, where granulation tissue gradually replaces the clot and develops terminally into fibrous tissue with obliteration of the vessel, waste products being carried off by the leukocytes in the venous or lymphatic stream.<sup>9</sup> With all the arterial longitudinal vessels crossing the site of the fracture blocked by thrombi and in progress of obliteration, any blood supply from them to the seat of fracture is impossible. The clot between the fragments, however, is gradually replaced by granulation tissue,<sup>10</sup> which results in a close network of thin-walled vessels. These vessels become thicker by the growth of adventitial cells, some of the connective tissue and others of the plasma cell group; thus fibrous tissue develops progressively. Obviously, at this time there is little help in repair given by the arterial vessels of the cortex, which are plugged by thrombi. The granulation tissue starts from buds from functioning vessels. These may be from the medullary cavity, but they are mostly from the area surrounding the fracture,<sup>11</sup> where the greatest activity,

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8. Kolodny, A.: The Periosteal Blood Supply and Healing of Fractures, *J. Bone & Joint Surg.* 5:698 (Oct.) 1923.

9. Keen, W. W., and DaCosta, J. C.: *Surgery, Its Principles and Practice*. Philadelphia, W. B. Saunders Company, 1920, vol. 1, p. 418; vol. 2, p. 104; vol. 5, p. 165.

10. Blaisdell and Cowan (footnote 6). Bancroft and Scudder (footnote 2, p. 927). Eising, E. H.: Remarks of the Physiology of Bone in Relation to Bone Diseases, *Am. J. Surg.* 3:368, 1927.

11. Bancroft and Scudder (footnote 2, p. 927).

## NORMAL BLOOD SUPPLY OF BONE

The outer layers of the long bones are nourished by the periosteum; the inner layer, by the medulla. Blood vessels run longitudinally through the bone in a series of canals called the haversian canals, around which the bony lamellae are grouped. Another series of vessels passes from the periosteum into the interior of the bone through minute orifices. The medullary or nutrient arteries enter the bone through the periosteum and, traversing the cortex at a sharp angle, enter the medullary cavity, the length of the artery in the cortex being relatively short. The epiphysis is supplied from vessels which anastomose around the joints from three sets of vessels: the diaphyseal, the metaphyseal and the epiphyseal; thus epiphyseal vessels communicate with those in the metaphysis,<sup>4</sup> and as the ramifications of the medullary or nutrient artery connect with the vessels in both the compact and the cancellous bone, anastomoses exist among all the arterial vessels in a bone. Johnson<sup>5</sup> maintains that the metaphyseal arteries are second in importance to the nutrient arteries in nourishing the medulla; the inner half of the cortex receives its nutrition from the medulla, and the outer half of the cortex is nourished by the periosteal vessels.

The periosteal blood vessels subdivide rapidly before entering the cortical bone. As the blood vessels enter the haversian and Volkmann's canals, they are surrounded by delicate sheaths of areolar tissue; through continuity with the endosteal arcade, this areolar tissue is attached to the wall of the canal, and this gives support to the more or less centrally located vessels.<sup>6</sup>

The veins and lymphatics are probably no less important to the healing of fractures than are the arteries. The veins emerge from the bone in three places: (a) one or two large veins accompany the medullary (or nutrient) artery; (b) numerous large and small veins emerge at the articular extremities, and (c) many small veins pass out from the compact substance.<sup>7</sup> Lymphatic vessels have been traced by Cruikshank into the substance of the bone, and Klein describes them as running in the haversian canals.<sup>7</sup> A point that one should keep in mind is that when bone is divided, its vessels do not contract into the canals in which they are contained.<sup>7</sup>

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4. Boyd, W. M.: *Surgical Anatomy*, Philadelphia, W. B. Saunders Company, 1925.

5. Johnson, R. W., Jr.: *A Physiological Study of the Blood Supply of the Diaphysis*, *J. Bone & Joint Surg.* 9:153 (Jan.) 1927.

6. Blaisdell, F. E., and Cowan, J. F.: *Healing of Simple Fractures*, *Arch. Surg.* 12:619 (March) 1926.

7. Gray, Henry; and Lewis, W. H.: *Anatomy of the Human Body*, Philadelphia, Lea & Febiger, ed. 21, 1924, p. 87.



Henderson and Brink<sup>14</sup> demonstrated this in 1908 by carefully conducted physical experiments. While muscle changes its shape in contracting and expanding, it does not change its volume. Since muscle is a colloidal solution, albeit retained in its form by its sheath or its other fibrous interstitial structures, it will have the physical characteristics of a fluid. In the case of a fracture of a long bone, pressures are created against and in the muscle: (1) by displacement by hemorrhage, (2) by hemorrhage into its own interstitial structure from the trauma which caused the fracture and (3) by infiltration of inflammatory products around and into the muscle tissue. This increase in volume is apparent as swelling and is not in itself harmful or prejudicial to repair of a fracture; however, if such swelling is prevented, a series of maladjustments in pressures ensue which are deleterious not only to the circulation to the fracture, but to the muscle tissue itself. As an example of the latter, ischemic paralysis may be mentioned. In this article, only the effects of pressure on the circulation of the fracture are considered. It has been shown how pressure in and about muscles is created; this pressure may be resisted by heavy layers of fascia and by tightly applied splints, bandages, adhesive plaster or casts. If resistance to expansion (swelling) occurs, its effect will be to diminish or occlude the lumen of the arterial blood vessels and thus prevent an adequate supply of blood from reaching the interior of the callus. I believe that, regardless of the exact manner in which mineral salts are laid down, they are carried by the arterial system to the region in process of repair. If this belief is correct, interference with an adequate supply of blood must have a deleterious effect. It will be shown subsequently that granulation tissue is converted into fibrous tissue, which, by its inherent power of contraction, eliminates the very vessels by which it was formed. If, however, sufficient bone tissue has been laid down while the new vessels were still patent, they will make a more or less permanent connection with the general circulation and persist through the period of their need. Hence the great importance of an effort to prevent considerable hemorrhage and inflammatory reaction even during the early days of a fracture is evident, or if this should occur, the immediate provision for the additional expansion by a readjustment of any circumferential dressing whether it is a bandage, cast or adhesive plaster.

While a generalized pressure of surrounding tissues may occlude the arterial part of the circulation to a fracture, it has the opposite effect on the veins and incidently also on the lymphatics. These vessels are provided with valves which, not allowing a backward flow, cause the thin contained fluid (blood or lymph) under pressure to move in only one

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14. Henderson, L. J., and Brink, F. N.: The Compressibilities of Gelatine and Solutions of Muscle, *Am. J. Physiol.* 21:248 (Feb.) 1908.

the most active circulation and the greater area exist. At about this stage, then, the clot is reduced in volume and is undergoing organization. It consists essentially of a moist, gluey weld of extraordinary adhesiveness. The new growth of vessels is horizontally<sup>12</sup> inward and no doubt horizontally outward from the medulla, providing, of course, in the case of the latter, that the injury has not entailed the destruction of the blood supply of the medullary cavity. Kolodny believes that "the endosteum is not able to participate in the callus formation until the intraosseal blood circulation recovers by formation of an anastomosis between the central portion of the nutrient artery and the metaphyseal blood vessels."<sup>8</sup>

#### EFFECT OF CUTTING THE VEINS AND LYMPHATICS AT THE SITE OF FRACTURE

The same shearing force that cut the arteries also must cut the veins and lymphatics, and as reposition of the fragments is practically never so accurately made as to bring the cut ends of the vessels into venous alignment, the flow of venous blood and lymph will not be reestablished across the fracture in the vessels except by the probable development of new vessels; however, this will not interrupt the carrying capacity of the veins and lymphatics, as will appear. While the cut arterial vessels are thrombosed to their nearest functioning collateral, the veins seldom are. The venous circulation has for its motivation: (*a*) the propulsive power of the heart, (*b*) the compressive effect of muscle action and (*c*) the suction from the thorax and the heart itself.<sup>13</sup> The propulsive power of the heart on the venous column, slight in any case, is of course nonoperative in the cut vessels, but the suction from the thorax and heart and the pressure of surrounding parts are still present. The valves in the veins and lymphatics prevent any flow of venous blood or lymph in any direction except toward the heart. Smaller veins (of less than half an inch, such as lie in bone) do not have valves.<sup>7</sup>

#### INCOMPRESSIBILITY OF MUSCLE TISSUE AND THE PROBABLE EFFECT OF THIS ON THE CIRCULATION OF BLOOD TO A FRACTURE AREA

There can be no doubt concerning the relative incompressibility of muscle tissue. Only by great pressures (those tremendously in excess of any existent in the body) can any compressibility be demonstrated.

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12. Wieder, Henry S.: *Regeneration of Bone*, Univ. Penn. M. Bull., 1907, p. 33.

13. Tigerstedt, R.: *A Testbook of Physiology*, ed. 3, New York, D. Appleton & Co., 1906, p. 19. Starling, E. H.: *Principles of Human Physiology*, ed. 4, Philadelphia, Lea & Febiger, 1926, p. 872.

## THE LAYING DOWN OF LIME SALTS

The deposition of mineral salts to form hard bone involves a different group of phenomena from those under consideration in this article. The theory that the osteoclasts and osteoblasts have the particular property of tearing down and building up bone does not have the universal recognition today that it did ten years ago,<sup>17</sup> although many writers still accept it. It has been shown that the formation of new blood vessels is mostly horizontal, and that the new trabeculae are arranged in the same direction. Ely<sup>18</sup> and later Blaisdell and Cowan<sup>6</sup> found, in their experiments on animals, that new bone was first laid down in the angle formed by the bone and the raised periosteum. This is the place where one would expect that anastomosis would first take place between the periosteal circulation and that in the cortex of the bone. It is also the place where the effect of motion between the fragments would be minimized as being farthest from the place of shearing action.

## DEVELOPMENT OF FIBROUS TISSUE

The result of the failure of bony union, with all it implies concerning the impossibility of reconstruction of the architecture of the normal bone, is a fibrous union between the fragments. The fact has been mentioned that granulation tissue replaces the blood clot following a fracture. Granulation tissue develops ordinarily into fibrous or scar tissue. In a small wound, this development will take place quickly and almost at the same time throughout the small area; but in a large wound, the process will be progressive and farthest advanced at the place where the granulation tissue started to bud or form. In the case of most large wounds, this will be at the periphery so that the progressive healing is from without inward, or as J. Renfrew White<sup>19</sup> put it, centripetally. In the case of a fracture, there are two bases from which the granulation tissue may start to form; these are the outer periphery of the clot, with which the periosteum is usually associated, and the medullary region, providing, in the case of the latter that the blood supply to this region has not been stopped. With a proper clot and no interruption to its vascularization and the laying down of mineral salts, bone healing will be carried out. When interruption of the continuity of the vessel system takes place,

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17. Eising (footnote 10, third reference). Arey, L. B.: The Origin, Growth and Fate of Osteoclasts and Their Relation to Bone Absorption, *Am. J. Anat.* 26: 315, 1919-1920. Watt, J. C.: Deposition of Calcium Salts in Areas of Calcification, *Arch. Surg.* 10:990 (May) 1925. Bancroft, F. W.: Bone Repair Following Injury and Infection, *Arch. Surg.* 5:646 (Nov.) 1922.

18. Ely, L. W.: Experimental Study of the Healing of Fractures, *Arch. Surg.* 5:527 (Nov.) 1922.

19. White, J. R.: Chronic Traumatic Osteomyelitis, New York, Paul B. Hoeber, 1919, p. 28.

direction; this, of course, is toward the heart and away from the fracture. It may also be remembered that the venous and the lymph streams are subject to a suction action by the thorax and heart. It would seem not unreasonable to presume that these factors acting together might create a negative pressure in the venous lymphatic channels in the bone, sufficient to carry off waste products, even if of little magnitude. There is plenty of evidence that in the tearing down process of the old bone, the products are carried away by the old vessels, that is, those running in a vertical direction. As evidence of this, there are the clear vertical spaces (erosion) shown in the old bone; one sees this in the cuts of sagittal sections of repairing bone, and it has been shown particularly in many articles on the subject of bone repair, for example, by Johnson,<sup>15</sup> by Todd and Her,<sup>16</sup> by Wieder<sup>12</sup> and by others. The eburnation so regularly (though not invariably) seen in cases of nonunion would seem to be a point in favor of believing that in these cases resorption of bone salts and other substances is through the veins and lymphatics.

#### RELATION OF NEW BONE TRABECULAE TO BLOOD VESSELS

The arrangement of the new trabeculae at the zone of fracture is at right angles to the cortex rather than parallel to it as in normal bone. This is presumably due to the fact that, in general, the new blood vessels growing into the original granulation tissue were derived from the surrounding soft tissues outside the bone and from the medullary cavity. The realinement of the vessels of the cortex is not complete for a year or more after the injury.<sup>3</sup> Delafield and Prudden, speaking of the ossification of osteophytes, said:

The blood vessels from which the pathological bone develops grow out of old vessels, and as in the formation of granulation tissue, are irregularly arranged and are subject to a variety of nutritive conditions, so that new bone is usually formed, not in a series of definite lamellae but in a series of irregular spicules or masses.<sup>16</sup>

Blaisdell and Cowan<sup>6</sup> have stated: "The manner of branching and the position of the blood vessels determine the form, position and manner of continuity of the early trabeculae." The progressive change in the direction of the trabeculae from the horizontal to the vertical is probably due to gradual changes in the anastomotic formation of the blood vessels (particularly of the arteries) by virtue of which they (the trabeculae) tend to conform to the direction of the vessels of the bone as a whole.

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15. Todd, T. W., and Her, D. H.: *The Phenomena of Early Stages of Bone Repair*, Ann. Surg. 86:715, 1927.

16. Delafield, Francis, and Prudden, T. M.: *A Textbook of Pathology*, ed. 12, New York, William Wood & Company, 1923, p. 1059.

exigencies of the process. Repeated injury to this delicate anastomotic network through motion of the fragments makes necessary repair by the formation of new vessels; this involves retardation in the interior of the callus while at the periphery granulation tissue is progressing to fibrous tissue; the latter contracts in due time and thus reduces the flow of blood to the interior of the callus. As a result, there is delayed or fibrous union.

Since muscle tissue is incompressible (by ordinary pressures), the addition of the volume of the hemorrhage and inflammatory exudate may reduce the lumen of the arterial supply either directly or indirectly by the transmission of pressures throughout adjacent muscles in accord with well known laws of hydraulics.<sup>20</sup> This is particularly likely to occur in the presence of resistance to expansion or swelling from fascial planes and circular bandages or casts.

The circulation through the veins and the lymphatics is of equal importance to that in the arterial system, because through their medium the old structure is torn down or resorbed, thus permitting the growth of new vessels to form and establish anastomoses which are essential to bone repair. Interruption to the flow of venous blood and lymphatic fluid by the same pressure that may retard the arterial supply does not occur because a generalized pressure on the veins and lymphatics forces their contained fluid toward the heart.

#### CONCLUSIONS

Whether or not there are any systemic causes for delayed union and nonunion of fractures, there would seem to be ample reason to believe that the consistent use of methods of treatment of fractures that require (1) good apposition, (2) adequate provision for expansion of surrounding structures and (3) freedom from any shearing or hinge motion between the fragments will be rewarded by a much lessened morbidity percentage. Good apposition is, of course, routine and needs no word of defense. Ample provision for expansion is not always provided in the cast, splint or other device used. Too much emphasis cannot be laid on the importance of splitting or bivalving the cast or in maintaining a constant watchfulness over circumferential bandages that they may never be too tight. A bandage may be correct at the time of its application, but over night, from the restlessness of the patient or from his having had the injured part in a dependent position, the limb may have swollen until the bandages are tight.

Much can be done at the first dressing to prevent excessive hemorrhage and inflammatory reaction. Usually at this time one is dealing

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20. King, H. W., and Wisler, C. O.: *Hydraulics*, New York, John Wiley & Sons, 1922, p. 7.

however, the normal bone repair will be interrupted or fail completely, and the characteristic fibrous union will occur. It has been said that the granulation tissue leading to vascularization starts on the periphery of the clot and possibly in the medullary cavity. From these places it is progressively inward and outward. The horizontal series of new arterial vessels may have its continuity interrupted by cutting from the shearing action of the two fragments if moved, and in practice this is done by too frequent or not sufficiently gentle, firm handling in dressing, or it may occur from lack of proper support by the splint, the adjustment of which may permit hingelike motion between the fragments. I cannot see any reason for the belief held by some that "a little motion is good for a fracture"; by this is not meant the gentle contractions of muscle, as, for instance, the motion by the fingers in a forearm fracture, the effect of which is to accelerate the supply of blood to the fracture and to facilitate the elimination of waste by the veins and lymphatics.

If the continuity of the vessels is broken, it will not stop the normal histologic progress of granulation into fibrous or bone tissue at the periphery of the healing area, but only in the newly injured area between the fragments; therefore, the development of granulation into fibrous and perhaps even bone tissue will continue here (at the periphery), while the central area must have its vessel system repaired before it can again take part in the normal process of repair, namely, vessel formation, laying down of lime salts, etc. The inevitable tendency of granulation tissue is to form fibrous tissue, which contracts and deprives this central area of its blood supply; without this, it cannot make the necessary repair of its continuity. No doubt, occasional damage to the new vessels between the fragments is repaired without prejudice to the final result, but if such damage is repeated too often, it may result in deprivation of blood supply to this area through the gradual occlusion of the peripheral vessels of the callus by the formation of fibrous tissue.

#### SUMMARY

The deposition of lime salts incident to the repair of a fracture is dependent on an adequate circulation in the callus.

Following a fracture, a new set of arterial vessels transverse to the long axis of the (long) bone is developed. These vessels arise by a process of budding, starting, for the most part, at the periphery of the injured area; it must be admitted, however, that in the absence of obstruction to the medullary vessels, such budding may also arise from them. An anastomotic arterial system is thus established, and through its medium the trabeculae are laid down, at first transverse to the long axis of the (long) bone but later obliquely and eventually vertically, as is normal, this being brought about by the ever changing anastomoses of the vessels. The lime salts are removed and replaced according to the

# STUDIES IN INTESTINAL OBSTRUCTION

## IV. STRANGULATION OBSTRUCTION: A COMPARISON OF THE TOXICITY OF THE INTESTINE AND OTHER TISSUES AUTOLYZED IN VIVO AND IN VITRO \*

OWEN H. WANGENSTEEN, M.D., PH.D  
AND  
GEORGE W. WALDRON, B.S.  
MINNEAPOLIS

In both the patient and the experimental animal, strangulating types of obstruction are the most serious. In addition to the occlusion of the bowel in strangulation obstruction a segment of intestine is deprived of its blood supply. The poorer prognosis and quicker fatal issue in such instances are due to the injury of the strangulated loop.

A study of strangulation obstruction, therefore, resolves itself into an inquiry into the autolysis of injured segments of intestine. It has been demonstrated in another study<sup>1</sup> that segments of intestine deprived of their blood supply undergo a rapid autolysis, with the liberation of toxic substances. In a few dogs in which strangulation obstructions had been established and the strangulating mechanism released a few hours later, death occurred, apparently caused by the absorption of toxic bodies from the strangulated segment. Autolysis of the segment to which the blood supply had been interrupted, rather than absorption from the lumen of such a segment, appeared to be responsible for the fall in blood pressure and the lethal issue observed in such animals on releasing the constriction of the strangulated segment.

In this investigation, comparisons have been made of the toxicity of various tissues when deprived of their blood supply. A study of the nonprotein nitrogen of the blood and urine has also been made in a number of these animals to note whether the autolysis of devitalized tissue would provoke the same alterations in the chemistry of the blood and urine as are observed in simple occlusion of the upper part of the intestine. An effort has also been made to ascertain whether the subcutaneous administration of sodium chloride to animals in the peritoneal cavities of which tissues were allowed to autolyze afforded the animal any protection.

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\* From the Department of Surgery of the University of Minnesota.

\* Presented before the Minnesota Pathological Society, April 19, 1927.

1. Wangenstein, O. H., and Loucks, M.: Studies in Intestinal Obstruction:

II. The Absorption of Histamine from the Obstructed Intestine, Arch. Surg. 16: 1089 (May) 1928.

with the break before the muscles have become spastic; there is only moderate swelling, and replacement of the fragments may be possible. The part should be placed in the position of election. Thus a fracture of the elbow if seen shortly after its occurrence may be placed in acute flexion with little danger of excessive swelling subsequently, and in fractures of the lower leg, the foot may be turned in. It is unnecessary and contributory to excessive swelling for one to endeavor to make an exact diagnosis by manipulation; roentgen-ray examination should follow the first dressing as soon as possible and readjustment of any deformity shown may then be made as soon as convenient, after which the roentgen ray should be employed to verify the position of fragments.

The fracture appliance, of whatever type, should not permit of any motion of the bone at the site of the fracture. The old rule to splint the proximal and distal joints is a good one.

Fractures should not be dressed frequently, unless the cause is imperative, and in dressing should be handled firmly and gently so that there is no motion between the fragments.

Open operations should be so planned and conducted as to minimize the damage to the surrounding circulation. The use of a tourniquet is not advisable, since with it, one is not cognizant of the amount of damage being inflicted on the circulation. Fibrous tissue about the fragments should be removed and likewise eburnated bone which is too compact to permit formation of new vessels with the consequent anastomotic phenomena so important in repair of fractures.



weight being 63.5 Gm. The average weight of the dogs into the peritoneal cavities of which loops of bowel were placed was 37 pounds (16.8 Kg.). The dog that recovered weighed 25 pounds (11.3 Kg.) and the segment of intestine, 52 Gm.

The four dogs into the peritoneal cavities of which pieces of liver were placed died. In one animal, the small lobe of the liver near the gallbladder was detached and dropped into the peritoneal cavity; at autopsy, there was no indication that bleeding had occurred from the liver. In the other animals, the pieces of liver used were obtained under sterile precautions from normal dogs killed during the course of another experiment. Three of these dogs weighed 35 pounds (15.9 Kg.) and the other 25 pounds. The weight of the segments of liver used averaged 56 Gm. One animal into the peritoneal cavity of which 35 Gm. of liver was placed, lived five days. The other three animals survived a little less than twenty-four hours. Three of the four dogs were given saline solution subcutaneously.

Of twelve dogs in which the animal's own spleen was detached from its source of blood supply and dropped into the peritoneal cavity, eight died and four recovered. The weights were not obtained in some of these animals, but there did not appear to be any uniformity between the size of the spleen, the weight of the dog and recovery. One animal weighing 26 pounds (11.8 Kg.) recovered following detachment of a spleen that weighed 82 Gm. Another dog that weighed 21 pounds (9.5 Kg.) died two days following the detachment of its spleen, the weight of which was only 22 Gm. Six dogs were given salt solution subcutaneously. One dog was given water subcutaneously. Post-operative treatment was not given to the remaining five animals. Of the four dogs that recovered, all were given saline subcutaneously. The average length of survival following the operative procedure on the other dogs was three and a half days.

A kidney removed from other healthy dogs was placed in the peritoneal cavity of two dogs, each weighing 25 pounds. The weights of the kidneys used were 34 and 29 Gm., respectively. One of these dogs died eighteen days later from a suppurating abdominal wound; the other dog made a permanent recovery. Two kidneys were placed in the peritoneal cavity of a third dog. The combined weight of the two kidneys was 60 Gm. This dog also survived the procedure. The employment of tissue obtained from another animal did not seem to be of any special handicap in recovery.

In order to establish better quantitative comparisons of the toxicity of various tissues in the process of autolysis, pieces of tissue weighing from 30 to 60 Gm. were removed under sterile precautions from two dogs killed with ether. The pieces were placed in sterile bottles with wide mouths containing about an equal weight of physiologic sodium

## METHOD

All surgical procedures were performed under ether anesthesia and aseptic technic. Blood was obtained from the jugular vein or the vein on the outer aspect of the hind leg of the dog. The blood urea was determined according to the method of Van Slyke and Cullen<sup>2</sup> and the blood chlorides after the method described by Gettler.<sup>3</sup> A number of the animals were kept in metabolism cages. The urine was collected and the nonprotein nitrogen determined by the micro-Kjeldahl method of Folin and Denis.<sup>4</sup> When sodium chloride was given, it was administered subcutaneously with a 50 cc. syringe; 400 cc. of a 2 per cent sodium chloride solution being given once daily. Segments of small intestine about a foot or a little more in length, weighing from 46 to 75 Gm., were removed from one dog and placed in the peritoneal cavity of another. In four instances, the loop was irrigated successively with water, alcohol, ether and water, until the contents were returned clear. About 2 liters of fluid were used in the irrigation of each loop. A large needle was inserted in one end, and the other end was left open. Irrigation was performed with a 50 cc. syringe. A few inches of both ends of the segment of intestine, where the irrigation was less effective, were cut off before the remainder of the segment was deposited in the peritoneal cavity of the other dog. In the other eight instances, following this irrigation, the bowel was slit on its antimesenteric border and the mucous surface painted with phenol in certain areas in order to destroy the mucous membrane. The destroyed mucosa was then scraped off with a knife. In a few instances, a major part of the mucosa was stripped off in this manner leaving only islands here and there.

The spleen was detached from its blood supply and dropped into the free peritoneal cavity in a number of animals. The same procedure was carried out with pieces of liver. The pancreas excised from other dogs was placed in the peritoneal cavity in two animals, and in a few animals kidneys excised from other dogs were used in the same way.

The twelve dogs from which segments of intestine were removed recovered following the establishment of the continuity of the intestinal tract by lateral anastomosis. Death occurred in eleven of the twelve animals into the peritoneal cavities of which the twelve segments of intestine were deposited. One dog recovered; in this animal, a good portion of the mucosa had been removed. Another animal lived seven days. Five dogs survived the procedure two days. The others died on the day following operation. One of the latter died in convulsions, a mode of death not uncommon in the rats injected intraperitoneally with the intestinal contents of either a dog or a rabbit. Two of the dogs that were given salt solution subcutaneously died the day following the placing of the intestinal loop into their peritoneal cavities. The heaviest segment of intestine weighed 75 Gm., the lightest 46 Gm., the average

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2. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease and Its Use for Rapid and Accurate Determination of Urea, *J. A. M. A.* **62**:1558 (May) 1914.

3. Gettler, A. O.: A Method for the Determination of Death by Drowning, *J. A. M. A.* **77**:1650 (Nov.) 1921.

4. Folin, O., and Denis, W.: Nitrogen Determinations by Direct Nesslerization; I. Total Nitrogen in Urine, *J. Biol. Chem.* **25**:473, 1916.

placed in the peritoneal cavity. In the body cavity the rate of autolysis would be somewhat increased because of the simultaneous action of living tissue in aiding the disintegration of the dead tissue. Table 1 shows the results of such injections, the results checking closely with those obtained previously when the same tissues were placed in the peritoneal cavity.

#### COMMENT

When the loops of the bowel removed from one dog and made bacteria-free by mechanical cleansing and irrigation with antiseptic solutions are placed in the peritoneal cavity of another animal, death quickly supervenes as a consequence of autolysis of the segment of intestine deprived of its blood supply. Such segments of bowel, averaging 63.5 Gm. in weight, were placed in the peritoneal cavities of twelve dogs. Only one recovered; in this animal, a considerable portion of the mucosa had been scraped off. In two animals, a portion of the mucosa was removed from the segment of bowel, and each of the dogs into the peritoneal cavities of which the prepared segments of bowel were placed was given 400 cc. of a 2 per cent sodium chloride solution subcutaneously. Both dogs died the next day.

Four dogs died after pieces of liver averaging 56 Gm. were placed in the peritoneal cavities. A salt solution was given subcutaneously to three of these animals, but without avail.

Kidney tissue removed from other dogs was placed in the peritoneal cavity of three dogs. One death occurred eighteen days later from a suppurating abdominal wound; the other two animals recovered. Saline solution was not given to any of these animals.

Death occurred in eight of the twelve dogs in which the spleen was detached from its source of blood supply and dropped into the peritoneal cavity. Six of the twelve dogs were given salt solution subcutaneously; the four dogs that recovered belonged to this group. The five dogs to which salt solution was not given subcutaneously died, as did the animal given water subcutaneously.

The postmortem pictures of the animals that died following deposition of segments of intestine and pieces of spleen or liver in their peritoneal cavities were much the same. Three or four hundred cubic centimeters of a brownish or serosanguineous fluid was usually present, and the peritoneal surfaces were reddened. The tissue placed in the peritoneal cavity could frequently not be identified other than as a friable, mushy mass. When the animal died the day after the operative procedure, or on the following day, the tissue was often spongy and contained gas. A fibrinous-like exudate was found uniformly about the tissue introduced. Cultures were made in several instances. In a number of these cultures *B. coli* were grown.

chloride, and the bottles were then placed in the incubator. At twenty-four, forty-eight, seventy-two and ninety-six hours following the incubation, a few cubic centimeters of fluid was aspirated from the bottles and injected intraperitoneally into rats. A sufficiently large number of

TABLE 1.—Results of Injection of Autolyzed Tissue After Sterilization

Tissue	Hours Incubated	Amount Injected, Cc.	Result	Remarks
Kidney	24	18	Recovery	Mildly ill
	48	12	.....	Died 2 days later
	48	10	Recovery	Fairly ill
	72	5	Recovery	Stuporous, but recovered
	96	10	Died	Mildly ill after injection; died 2 days later
	4 months	4	Died	Convulsions 10 minutes after injection
Spleen	24	15	Recovery	Mildly ill
	48	12	Recovery	Mildly ill
	48	10	Recovery	Mildly ill
	72	5	Recovery	Stuporous, but recovered
	96	10	Died	In convulsions 5 minutes after injection; convulsive seizures for 45 minutes; died next day
	4 months	4	Died	Very ill; died during night
Liver	24	15	Died	Moderately ill; died during night
	48	12	Died	Moderately ill; died during night
	48	10	Recovery	Fairly ill
	72	5	Died	Stuporous; found dead in a.m.
	96	10	Died	Not as ill as other animals injected with 4 day tissue culture; died 2 days later
	4 months	4	Died	Stuporous; died 12 minutes later
Pancreas	24	15	Died	Dead 20 minutes after injection
	48	12	Died	Died during night
	48	10	Died	Died during night
	72	4	Recovery	Stuporous following injection
	96	10	Died	Moderately ill after injection; died 2 days later
	4 months	4	Died	Convulsions; dead in 5 minutes
Duodenum	24	17	Died	Dead 30 minutes after injection
	48	12	Died	Died during night
	48	10	Died	Died during night
	72	5	Died	In convulsions 3 minutes after injection; dead 2 minutes later
	96	10	Died	Convulsive seizures; dead a few minutes after injection
	4 months	4	Died	Very ill; dead in 30 minutes
Jejunum	24	15	Died	Dead 7 minutes after injection
	48	12	Died	Very ill; died a few hours after injection
	48	10	Died	Very ill; died a few hours after injection
	72	5	Died	Stuporous; died during night
	96	10	Died	Convulsive seizures; dead 10 minutes after injection
	4 months	4	Died	Convulsions; died in 10 minutes
Stomach	24	18	Died	Dead 7 minutes after injection
	48	12	Died	Very ill; dead a few hours after injection
	48	10	Died	Very ill; dead a few hours after injection
	72	5	Recovery	Stuporous, but recovered
	96	10	Died	Convulsive seizures; dead 4 minutes after injection
	4 months	4	Died	Very ill; died in 20 minutes
Muscle	24	15	Recovery	Mildly ill
	48	12	Died	Died during night
	48	10	Died	Died during night
	72	5	Recovery	Stuporous, but recovered
	96	10	Died	Lethargic and stuporous; died during night
	4 months	4	Died	Convulsions; dead in 12 minutes

bottles were prepared so that each day's injection was made from a separate bottle. Injections of tissues autolyzed in this manner were made with liver, spleen, pancreas, muscle, kidney, stomach and intestine.

In the incubator, tissues would undergo about the same qualitative process of autolysis as the same tissue deprived of its blood supply when

TABLE 2.—*Toxicity of Various Tissues in Process of Autolysis*

Dog	Nature of Procedure	Day After Operation	Blood Mg. per 100 Cc.		Urine and Vomitus*			
			Urea	Chlorides	Amount	Nonprotein Nitrogen		
55	Spleen detached from blood supply 10/4/26; no saline	0	16.80	480	.....	.....		
		1	14	330	.....	.....		
		2	14.54	410	.....	.....		
		3	10.20	430	.....	.....		
		4	20.53	400	.....	.....		
		5	23.03	300	.....	.....		
Dog died 10/9/26								
59	Spleen detached from blood supply 10/12/26; 400 cc. 2% sodium chloride given once daily	0	15.83	430	.....	.....		
		1	15.40	450	.....	.....		
		2	12.60	430	.....	.....		
		3	13.00	530	.....	.....		
		4	17.73	400	.....	.....		
		5	11.20	430	.....	.....		
		Saline discontinued .....		6	14	400	.....	.....
		7	20.53	510	.....	.....		
		8	15.83	530	.....	.....		
		9	13.06	510	.....	.....		
		10	14.03	300	.....	.....		
Dog well		11	14.47	310	.....	.....		
113 Weight, 25 pounds (11.3 Kg.)	52 Gm. of intestine put into the peritoneal cavity 2/1/27; no saline	0	13.06	400	.....	.....		
		1	16.80	380	550	4.67		
		2	15.83	400	1,470	5.35		
		3	10.30	400	1,000	7.06		
		4	17.20	430	1,000	6.40		
		5	15.80	380	1,070	4.68		
		6	13.30	390	1,310	5.49		
		7	10.50	300	1,230	5.66		
		8	15.37	410	700	3.26		
Dog recovered		9	17.02	380	450	2.48		
121 Weight, 30 pounds (13.6 Kg.)	Two kidneys (60 Gm.) put into the peritoneal cavity 2/10/27; no saline	0	10.26	400	120	1.14		
		1	15.83	490	375	2.62		
		2	14.73	300	1,320	7.58		
		3	11.20	430	1,550	5.81		
		4	24.26	440	1,100	0.34		
		5	13.30	410	900	5.76		
		6	10.53	390	700	5.32		
		7	14.78	420	520	4.03		
		8	17.33	380	580	3.23		
Dog well		9	15.24	430	340	2.30		
117 Weight, 35 pounds (15.9 Kg.)	15 inch closed loop obstruction; continuity reestablished by lateral anastomosis 2/9/27; no saline	0	9	420	100	1.25		
		1	13.00	400	1,650	4.77		
		2	15.80	490	2,850	5.91		
		3	23.03	300	1,900	5.60		
Dog died 2/12/27; loop markedly gangrenous; perforations on antimesenteric border; bloody fluid in peritoneal cavity and in the closed loop								
126 Weight, 35 pounds (15.9 Kg.)	15 inch closed loop obstruction; continuity reestablished by lateral anastomosis 2/14/27; 400 cc. 2% sodium chloride once daily, discontinued on 2/17/27	0	14.70	430	110	1.02		
		1	12.00	410	2,800	4.40		
		2	16.80	420	4,700	5.95		
		3	10.33	300	1,900	5.36		
		4	14.47	610	475	4.41		
		5	15.40	490	500	4.61		
		6	13.52	450	340	3.27		
		7	20.53	440	370	3.06		
Dog moribund; killed 2/23/27; perforations and extensive gangrene of closed loop		8	24.20	410	260	2.57		

\* The dogs were allowed to drink water. They were starved for one day before being placed in metabolism cage and were not given food while in the cage.

"short circuiting" method for treating subjects with chronic intestinal obstruction. Experimental as well as clinical evidence has shown it to be decidedly unsafe. Perforations have been known to occur years after turning in the ends of such a loop. (Barracz, R.: Experimenteller Beitrag zur Frage der Totalen Ausschaltung mit totalem verschluss der ausgeschalteten Darm-schlinger zugleich Beitrag zur axialen Darmvereinigung, Arch. f. klin. Chir. 58: 120, 1899. Kammerer, F.: Bilateral Exclusion and Occlusion of the Intestine, Ann. Surg. 61:497, 1915. Wiesinger: Zur Darmausschaltung, Deutsche Ztschr. f. Chir. 100:1267, 1909.)

but with no greater regularity from the peritoneal cavity of the dogs in which intestinal segments had been placed than when liver or spleen was used.

In these experiments on the autolysis of various tissues in the peritoneal cavity, the liver and the intestine seemed to be the most toxic. Kidney tissue appeared relatively nontoxic. The disintegrating splenic tissue seemed intermediate in toxicity. The outcome in the dog in which the spleen was allowed to autolyze appeared to be affected favorably by the subcutaneous administration of salt solution. In the instances in which the liver and the intestine were placed in the peritoneal cavity, saline did not appear to have any value. It must be pointed out, however, that dogs with segments of intestine or liver in their peritoneal cavities lived only about a day, whereas the animals in which the spleens had been detached from the source of blood supply and which did not receive saline survived for more than three days.

When the autolysis was carried on *in vitro* in the incubator at 37 C. and the autolyzed tissue injected into the peritoneal cavities of rats at varying intervals, results of the same nature were obtained. The kidney and splenic tissues were definitely the least toxic. Bowel tissue, pancreas and liver appeared to be most toxic. The latter tissues seemed to disintegrate into toxic bodies more quickly than kidney and splenic tissue. After four days of incubation, the intraperitoneal injection of splenic tissue into a rat elicited marked symptoms. After four months' incubation, marked symptoms were elicited in all instances on injection. The injected substances appeared about equally toxic. Therefore, there would appear to be a qualitative difference in the toxicity of disintegrating tissues early in the process as well as a difference in the rapidity of autolysis.

Chemical studies of the urine of dogs in the peritoneal cavities of which tissues deprived of their blood supply were allowed to disintegrate showed a markedly increased excretion of nitrogen as was observed in the animals with simple occlusion of the intestine. The marked increase of blood urea nitrogen noted in animals with high intestinal obstruction was not observed in these; only slight increases in the nonprotein blood nitrogen were usually obtained.

Studies of the blood and urine nitrogen were also made in four dogs with irrigated obstructions of the closed loop in which the continuity of the intestinal tract had been reestablished by lateral anastomosis. These animals died from gangrene and perforation of the closed loop.<sup>5</sup> In three

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5. Sixteen of twenty-five dogs with irrigated closed loops on whom Dragstedt and his co-workers experimented lived for some time. Possibly, a longer loop would diminish the danger of gangrene and perforation. At one time it was thought that this was a safe way to dispose of segments of intestine in the

Duval and Grigault,<sup>11</sup> studying the disintegration of protein in traumatic shock, observed a moderate increase in the nonprotein blood nitrogen of patients in a state of shock. Aub and Wu<sup>12</sup> obtained only slight increases in the nonprotein nitrogen of the blood in animals suffering from true shock after marked muscle trauma. Hashimoto<sup>13</sup> obtained moderate increases in the nonprotein nitrogen of the blood in which histamine intoxication followed repeated subcutaneous administration of histamine. Whipple and his co-workers<sup>14</sup> noted the increased urinary excretion of nitrogen following proteose intoxication.

In these experiments when disintegration of the tissue occurred following autolysis of tissue in vivo, a marked increase in the excretion of nitrogen in the urine was observed, with only a slight increase of the nonprotein nitrogen of the blood. The low values for blood chlorides noted in dogs with simple obstruction of the upper part of the intestine were not obtained in these animals. The increased urinary excretion of nitrogen is due probably only in a small part to the actual disintegration of the autolyzed tissue; the destruction of the devitalized tissue in all likelihood precipitates the breakdown of other body protein.

In this connection, it is interesting to speculate as to the cause of the marked increase in the blood nonprotein nitrogen observed in animals with simple occlusion of the upper part of the intestine. There is no evidence to indicate that the injury of the kidney is greater in animals with simple obstruction than in those in which tissue is allowed to autolyze. The rapidity with which tissue breaks down following dehydration and loss of chlorides would not alone account for the accumulation of nonprotein nitrogen in the blood, especially as this increase is dissipated by the administration of saline. The giving of saline does not prevent the increased urinary excretion of nitrogen, nor does the nonprotein nitrogen in the urine of these animals given saline seem to be increased over that observed in the animals that do not receive salt. Marshall and Davis<sup>15</sup> have shown that nearly all tissues have about the same urea content as blood. If an increase in the nonprotein nitrogen of the tissues in these animals occurred commensurate with that observed in the blood, if saline actually washed out the increased nonprotein

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11. Duval, A., and Grigault, A.: L'intoxications par les plaies de guerre. La retention azotée des blessés, C. R. de soc. de biol. 81:873, 1918.

12. Aub, J. C., and Wu, H.: Studies in Experimental Traumatic Shock: Chemical Changes in the Blood, Am. J. Physiol. 54:416 (Dec.) 1920.

13. Hashimoto, H.: Blood Chemistry in Acute Histamin Intoxication, J. Pharmacol. & Exper. Therap. 25:381 (June) 1925.

14. Cooke, J. V., and Whipple, G. H.: Proteose Intoxications and Injury of Body Protein, J. Exper. Med. 28:223 and 243 (Aug.) 1918; *ibid.* 25:461 (March) 1917.

15. Marshall, E. K., and Davis, D. M.: J. Biol. Chem. 18:53, 1914.

dogs, isolated loops were similarly irrigated, although the ends were left open and lateral anastomoses made; these dogs recovered. A second operation was performed later on one of these dogs; the ends were found partially sealed. There was free fluid in the peritoneal cavity. The dog died following a free opening of this loop. When extensive gangrenous changes obtain in irrigated closed loops, strangulation of intestine has occurred minus the obstructive factor. In these animals, an increased urinary excretion of nitrogen was obtained, but the high blood urea observed in simple occlusion of the upper part of the intestine was not noted.

Corroboration of the rapid disintegration of strangulated intestine previously noted<sup>1</sup> when a segment was strangulated with its mesentery and the constriction subsequently released was observed when the intestine was allowed to autolyze in vivo in the peritoneal cavity, or when the products of autolysis were injected into the peritoneal cavity of rats after being incubated in vitro. Comparisons made with other tissues showed the products of autolysis of intestine to be markedly toxic. Mann,<sup>6</sup> in removing the liver in dogs, has observed that when a piece of liver two fingerbreadths in width remained free in the abdomen, the dogs died within sixteen hours. Mason and Davidson<sup>7</sup> also observed the marked toxicity of liver tissue allowed to autolyze in the peritoneal cavity. None of the fifteen dogs survived in which from 30 to 110 Gm. of liver tissue was placed in the peritoneal cavity. The usual period of survival following the operative procedure was about twenty hours. Only three<sup>8</sup> of six dogs died in which the spleen used weighed from 23 to 68 Gm. The post-mortem appearance of the peritoneal surfaces following the autolysis of tissue described in this paper was noted by these authors.<sup>7</sup> They also observed that the fluid present in the peritoneal cavity at death was much less toxic on injection than the autolyzing tissue itself.<sup>9</sup> Delbet and Karajonopoulos<sup>10</sup> made the same observation on muscle tissue autolyzed in vitro.

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6. Mann, F. C., quoted by Mason and Davidson: A Study of Tissue Autolysis in Vivo; I. Blood Changes, Physical and Chemical, *J. Lab. & Clin. Med.* 10:622 (May) 1925.

7. Mason, E. C., and Davidson, E. C.: *J. Lab. & Clin. Med.* 10:622 (May) 1925.

8. Mason, E. C., and Davidson, E. C.: A Study of Tissue Autolysis in Vivo; III. Observations Using the Spleen, *J. Lab. & Clin. Med.* 10:997, 1925.

9. Mason, E. C., and Davidson, E. C.: A Study of Tissue Autolysis in Vivo; 11. A Pharmacological Study of the Toxic Material, *J. Lab. & Clin. Med.* 10:906, 1925.

10. Delbet and Karajonopoulos: De la toxicite des autolysats musculaires au point de vue du choc, *Bull. Acad. de méd.* 80:13 (July) 1918.



# INTESTINAL TUBERCULOSIS CAUSING OBSTRUCTION \*

J. R. B. BRANCH, M.D.

PEKING, CHINA

From April, 1927 to April, 1928 eight patients with hyperplastic intestinal tuberculosis with obstruction of varying degrees were operated on in the surgical service of the Peking Union Medical College Hospital. The cases, some of which have been reported in a short article previously published, form the basis of this report.<sup>1</sup>

Intestinal tuberculosis associated with pulmonary tuberculosis has long been recognized. The importance of early diagnosis and treatment in this condition has been recently stressed in a monograph by Brown and Sampson.<sup>2</sup> In 1925, Larimore and Fisher<sup>3</sup> reported a series of cases of ulcerative processes in the cecum in which the patients were operated on with encouraging though not brilliant results. In an article on tumors of the secum Erdmann and Clark,<sup>4</sup> in 1927, reported seven cases of tuberculosis of the cecum and terminal ileum with symptoms of intestinal obstruction. In this series, the pulmonary observations were negative.

## FREQUENCY

Probably the most severe cases of pulmonary tuberculosis present some intestinal involvement; lesions are found in the intestinal tract of from 70 to 90 per cent of patients dying of this disease.<sup>5</sup> These lesions are usually of the ulcerative variety, and in only 25 per cent of them does stenosis or stricture develop;<sup>6</sup> it is during comparatively recent times that operation has been considered possible in such cases. The hyperplastic and stenosing lesions are more commonly treated surgically. In 100 cases of cecal lesions in which the patients were submitted to operation, Gant found four cases of hyperplastic tuberculosis; in Erdmann and Clark's series of forty-eight tumors of the cecum, seven were tuberculous.

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\*From the Department of Surgery, Peking Union Medical College.

1. Branch, J. R. B.: *The Surgical Treatment of Intestinal Tuberculosis*, China M. J. **42**:239 (April) 1928.

2. Brown, L., and Sampson, H. L.: *Intestinal Tuberculosis*, Philadelphia, Lea & Febiger, 1926.

3. Larimore, J. W., and Fisher, A. O.: *Tuberculosis of the Cecum*, Ann. Surg. **83**:496 (April) 1926.

4. Erdmann, J. F., and Clark, A. E.: *Tumors of the Cecum*, Ann. Surg. **85**:722 (May) 1927.

5. Fenwick and Dodwell: *Lancet* **11**:133, 1892.

6. Read, W. D.: *Tuberculosis of Cecum*, Northwest Med. **20**:282 (Oct.) 1921; *Cecal Pathology*, *ibid.* **20**:11 (Jan.) 1921.

nitrogen of the blood, an appreciable increase in the urinary excretion of nitrogen would be observed over that obtained in animals that did not receive saline. Water alone fails to obviate this increase in non-protein blood nitrogen. It would appear that an alteration in the permeability of tissue may occur in these animals such that the rapid dehydration and loss of chlorides incident to the obstruction may permit the accumulation of nonprotein nitrogen in the blood.

In the recovery of the animals following the detachment of the spleen and its autolysis in the peritoneal cavity after the subcutaneous administration of saline, it would appear that saline possesses a protective value in combating the toxemia accompanying the disintegration of tissue. It has been maintained that saline performs such a function in the treatment of burns.<sup>16</sup> In the foregoing experiments, however, factors such as the protective influence of the omentum must be controlled before the recovery of the animal is ascribed to saline alone. Evidence was not obtained that would indicate that the administration of saline was of any value in combating the toxemia that occurred when the intestine was deprived of its blood supply.

#### SUMMARY AND CONCLUSIONS

Comparisons have been made of the toxicity of intestine and various tissues on autolysis in vivo and in vitro. The products of disintegration of the intestine were found to be markedly toxic when segments of small intestine were allowed to autolyze in the peritoneal cavity or when rats were given intraperitoneal injections of the products of autolysis of intestine from sterile containers kept in the incubator. A marked increase in the urinary excretion of nitrogen was observed in the animals in which various tissues were allowed to autolyze; however, only a slight increase in the nonprotein nitrogen of the blood occurred. The low values for blood chlorides observed in dogs with obstruction of the upper part of the intestine were not obtained in strangulation of the intestine alone (closed loop obstruction with gangrene) when the continuity of the remainder of the intestinal tract was restored. The subcutaneous administration of saline to animals with disintegrating segments of intestine appeared to be valueless.

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16. Davidson, E. C.: Sodium Chloride Metabolism in Cutaneous Burns and Its Possible Significance for a Rational Therapy, *Arch. Surg.* 13:262 (Aug.) 1926.

mens showed a coexisting old infection with *Schistosoma* in the cecum and ileum, associated with tuberculosis.

The outstanding feature in all of the cases was a generalized thickening of the entire wall of the bowel with old, healed, scar tissue resulting in stenosis of the lumen; in several cases, the stricture was 5 mm. or

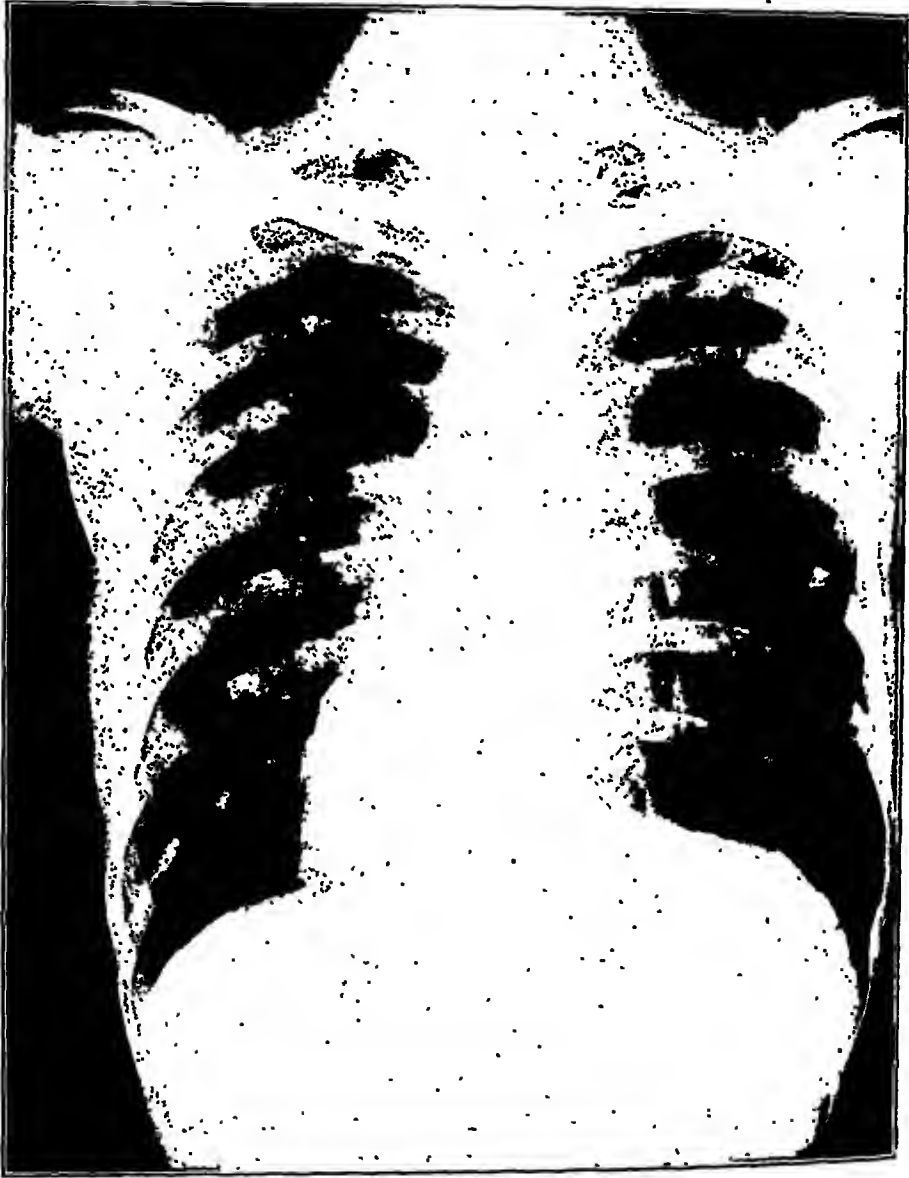


Fig. 1 (case 2).—Roentgenogram of the chest, July 19, 1927, showing thickening of apical pleura on the left side and fibrosed tuberculous infiltration of upper area on the right side. Lesions have not changed in six years.

less in diameter. The mucosa was thickened and often projected into the lumen as papillary elevations, some of them being from 1 to 2 cm. in length. Ulceration was not prominent, though in most of the cases small healed and unhealed ulcers were found. Grossly, little was seen

During the past five years, one of three resections of the right colon performed in this hospital was for tuberculosis. Within the past nine months, seventeen cases of intestinal tuberculosis have been seen on the medical service here, in which the condition was diagnosed by roentgen ray, but for one reason or another the patients were not transferred to the surgical service for operation. Although these figures are not intended to convey any information concerning the relative frequency of the condition in China, it is striking to see so many cases in Peking during one year. I did not encounter a case during twelve years spent in active surgical work in a clinic in Central China, though there must have been many in the community.

#### PATHOLOGY

About 85 per cent of the involvement in intestinal tuberculosis is in the terminal ileum, cecum and proximal colon.<sup>7</sup> Fifty per cent of the patients with tuberculous peritonitis have intestinal tuberculosis also, and 20 per cent of the patients having intestinal tuberculosis have peritoneal involvement as well.<sup>8</sup>

The type of lesion varies; in some instances, particularly when associated with pulmonary tuberculosis, it is ulcerative and progressive. This association with processes in the lungs and perhaps elsewhere is responsible for the term "secondary." Another type is the hyperplastic lesion, which is frequently called "primary." While it is true that in the latter variety there may not be any demonstrable tuberculous lesions in the lungs or elsewhere, and that from the data secured by physical examinations and roentgen-ray studies one may fail to find an original focus, it is, however, not only possible but highly probable that there may be or may have been processes elsewhere. Without complete examinations at autopsy, one is not justified in speaking of these cases as "primary."<sup>9</sup>

All of my cases were of the hyperplastic, stenosing variety, and the pathologic pictures were all strikingly similar (fig. 12). The lesions were in the terminal ileum, cecum and ascending colon; in several cases the appendix also was involved in the tuberculous process. Two were associated with tuberculous peritonitis, one in the ascitic and one in the early plastic stage. Three patients had evidence of previous pulmonary tuberculosis, but in only one was the process active. One of the speci-

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7. Powell and Hartley: *Diseases of the Lung and Pleura*. Philadelphia, P. Blakiston's Son and Company, 1921, p. 798. Blumberg, Alfred: *Pathology of Intestinal Tuberculosis*, *J. Lab. & Clin. Med.* 13:405 (Feb.) 1928.

8. Albrecht: *Ueber die Beziehungen zwischen peritoneal und genital Tuberculose*, *Verhandl d. deutsch.*

9. Charbrut, R.: *Sur les resultats de la resection dans la tuberculose ileo-caecale* (40 observations), *J. de chir.* 30:656 (Dec.) 1927.

in the numerous sections examined. When evidence of dysentery or other probable cause for the lesion is lacking, I am of the opinion, however, that the patient also had intestinal tuberculosis, and the case is accordingly included in this series.

In some instances glandular involvement was observed; it was extensive and marked in one case. The complete report of case 5 is given

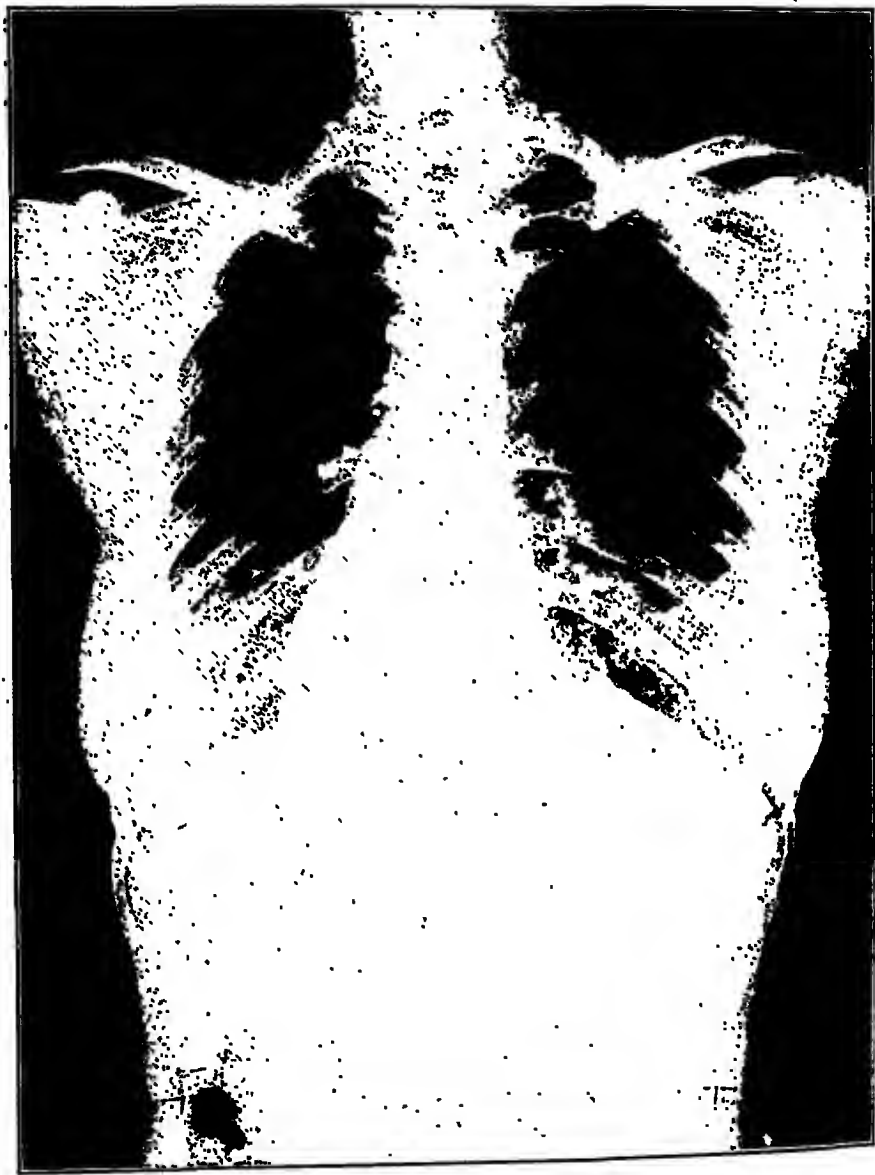


Fig. 3 (case 3).—Roentgenogram of the chest, Sept. 1, 1927, showing essentially normal lungs.

subsequently as typical of the observations in this series; the specimen removed at operation (ileum, cecum and ascending colon) is illustrated in figure 12.

to suggest more than a determined and successful reaction to combat a chronic infectious process, so that the pathologist was disinclined to agree with the clinical diagnosis of tuberculosis until sections were examined. The gross pathologic picture would have been the same if the causative agent had been dysentery, *Schistosoma* or any other chronic



Fig. 2 (case 2).—Roentgenogram, July 19, 1927, made six hours after ingestion of barium, showing dilatation of the terminal ileum, nonfilling of the cecum and incomplete filling of the ascending colon.

irritant. The condition in all cases with the exception of one was diagnosed as tuberculous on microscopic examination, tubercles and bacilli being demonstrated. In case 6, essentially like the others clinically, and with similar gross pathologic changes, tubercle bacilli were not found

showed many small and large papillary growths, varying in length from 0.1 to 1 cm. and in diameter from 0.1 to 0.3 cm. Near the papillary region, namely, in the large intestine, there were several grayish pink and dark red ulcers from 0.2 to 1 cm. in diameter. The mucosa in this region was swollen and elevated, and was a grayish white. The walls of the intestine varied from 0.3 to 2 cm. in thickness.

Sections of the small intestine examined microscopically revealed the irregularly thickened and edematous mucosa with infiltration by polymorphonuclear leukocytes, wandering cells, plasma cells and lymphocytes. Approximately in the center, there was a necrotic and hemorrhagic area which extended even into the submucosa. Elsewhere in the submucosa, marked edema and hemorrhage with infiltration by leukocytes was revealed. The muscularis was thickened in places and at one end showed edema with infiltration by a small number of leukocytes. Opposite the necrotic and hemorrhagic area, the muscularis was replaced by fibrous tissue with small and large blood vessels and infiltration of leukocytes. The serosa was thickened with a large amount of fat tissue and slight infiltration by leukocytes. In the mucosa, submucosa, muscularis and serosa, a few tubercles consisting of epithelioid cells and giant cells were present.

Sections of the large intestine showed that the mucosa was irregularly thickened and edematous with infiltration by wandering cells, plasma cells, lymphocytes and polymorphonuclear leukocytes. In places the submucosa revealed marked edema with infiltration by leukocytes. The muscularis was also irregularly thickened, and at one side areas of small and large intestinal glands were present, some of which were dilated and showed cystic structure, with lumina which were empty or contained a small amount of coagulated material, desquamated epithelium and many polymorphonuclear leukocytes. The muscularis was infiltrated with wandering cells, lymphocytes, plasma cells and polymorphonuclear leukocytes, especially surrounding those areas. Nearly a large tubercle consisting of epithelioid cells and giant cells was present. The serosa was also thickened and edematous with a large amount of fat tissue and infiltration by leukocytes. Sections of surrounding fat and fibrous tissue showed that many small and large tubercles consisting of epithelioid cells and giant cells were present. The tubercles were necrotic in a few places, containing dead cells and polymorphonuclear leukocytes, and were surrounded by lymphocytes and plasma cells. Elsewhere the fat and fibrous tissue also showed infiltration by lymphocytes, plasma cells, polymorphonuclear leukocytes and large cells with granular cytoplasm and oval or round nuclei in the center or near the edge. Here and there, slight hemorrhagic areas were also present. On careful examination only four tubercle bacilli were found. A diagnosis was made of tuberculosis of the cecum with stenosis of the lumen of the intestine.

#### CLINICAL PICTURE

My experience is similar to that of Erdmann, who stated that the condition in all of his seven cases had been diagnosed at various times as appendicitis. The patient in case 1 was operated on through a McBurney incision for appendicitis when the tuberculous cecum was found; in case 3 the patient had undergone appendectomy four months previously (the appendix was tuberculous); in case 5, exploration had been performed owing to severe, paroxysmal, abdominal pain thought to be due to a strangulated ovarian cyst; in the others, the condition at one time or another was thought to be appendicitis.

## REPORT OF CASE

At operation on a Chinese woman, aged 28, a specimen consisting of a portion of the small and large intestines, measuring 19 cm. in length and from 2 to 3 cm. in diameter, was obtained. Gross examination revealed a large amount of grayish, pink and light yellow fat and fibrous tissue attached to the external surface. The cut surface of the large intestine revealed an obstructive portion in which the lumen measured approximately 0.5 cm. in diameter. The mucosa in this region



Fig. 4 (case 3).—Roentgenogram of the colon, June 28, 1927, after injection of barium enema, showing nonfilling of the cecum, general narrowing of the ascending colon at its proximal portion, incompetence of the ileocecal valve and dilatation of the terminal ileum. Diagnosis of a hyperplastic and obstructive lesion (tuberculosis) of the ileocecal region and the ascending colon was made on this examination.



The physical, laboratory and roentgen-ray examinations are more illuminating. In my patients the chest either was normal or, as in three cases, showed old, healed, unimportant pulmonary lesions. In case 7 active lesions were seen. (These observations were confirmed by roentgen-ray films.) The abdominal examination did not reveal anything of importance except in the right iliac fossa; here localized, moderate tenderness was noted, but muscle spasm, involuntary resistance or rigidity was not present. In every case there was a mass in the cecal region which persisted after satisfactory enemas had been given. This mass had the limits of motility one might expect in the cecum, though in case 5 it could be pushed up to the costal margin and down to the pelvis. In one case with associated tuberculous peritonitis, the temperature was

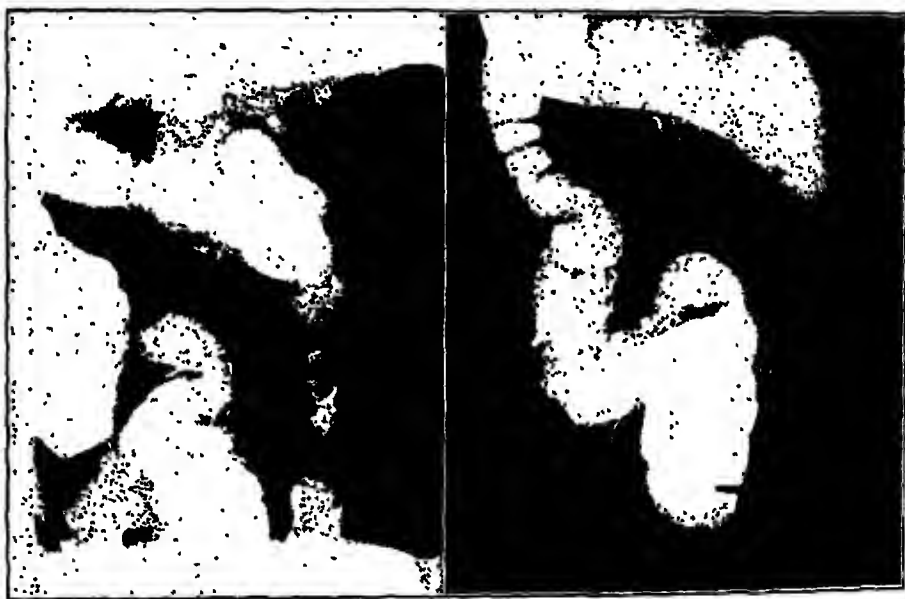


Fig. 6 (case 4).—Roentgenograms, Aug. 31, 1927, made under fluoroscopic control following injection of barium enema, demonstrating the different phases of filling of the cecum and the ascending colon due to active spasm of these parts.

39.2 C.; in another, it was 38.8 C., and in a third uncomplicated case, it was 37.4 C. In the other cases the temperature was normal. The leukocyte count was normal in all but two patients; the patient in case 6 had 11,000 white cells with 86 per cent polyphosphonuclears and the patient in case 7 had 14,400 white cells with 74 per cent polymorphonuclears.

The roentgen-ray studies were most important. In all of the cases, with the exception of the first, roentgen-ray examination was made of the intestinal tract. The fluoroscopic and roentgenographic observations were characteristic of either ulcerative or hyperplastic lesion and in every instance, with the exception of case 8, confirmed the clinical diagnosis of intestinal tuberculosis. The constant symptoms were: (1) filling defect—nonfilling, irregularity, narrowing and constriction; (2) gen-

The predominating symptom is abdominal pain, at times general, at other times localized in the right lower quadrant. It is described as colicky, recurrent and paroxysmal, and, in some instances, is exceedingly severe; gurgling of gas is frequently present in the bowels, and in every case there is nausea and vomiting. The attacks of pain in some cases lasted three or four hours, in others as long as seven or eight hours. Most of the patients gave a history of constipation, and some of them had had attacks of diarrhea. In the interim they either were well, or

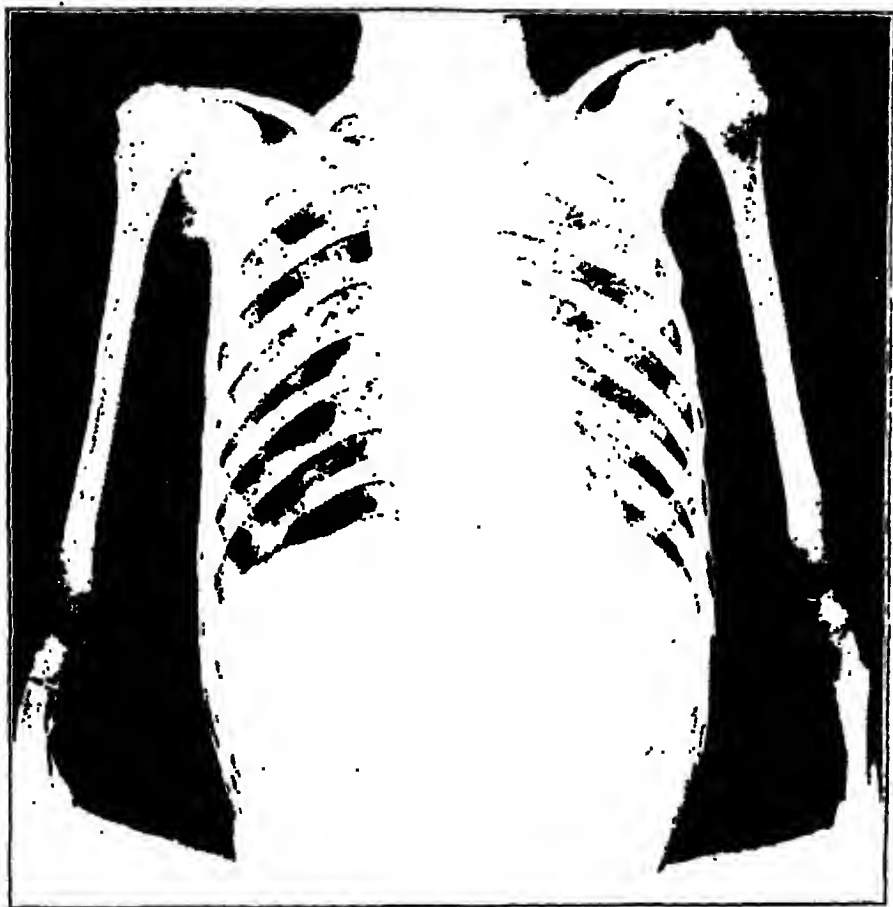


Fig. 5 (case 4).—Roentgenogram of the chest, Aug. 29, 1927, showing moderately increased thickening of the shadows of the hilum on both sides, which, in a subject aged 11 years, was thought to be of some clinical significance.

had vague abdominal discomfort; however, there was a definite tendency for the interval of freedom from attacks to become shorter and for the duration of the attacks to become longer. Such a symptom-complex would seem to indicate a pathologic process in the right lower abdominal quadrant, and one would naturally think first of the most common condition: appendicitis.

methods barium meal proved preferable because it provided the means of studying both the anatomic and the physiologic changes in the intestine, and, therefore, all the diagnostic signs, when present, could be seen. In all five cases in which the barium meal was employed, colonic hypermotility and ileal stasis, the cardinal sign-complex of ulcera-



Fig. 8 (case 5).—Roentgenogram, Nov. 11, 1927, made after the injection of a barium enema, showing filling defect of the cecum and ascending colon, incompetency of the ileocecal valve and dilatation of the terminal ileum.

tion, were present in addition to the filling defect of the cecum and, in some cases, the terminal ileum. Localized tenderness was present in three patients, and a palpable mass which corresponded to the poorly filled cecum was observed in all the patients.

eral colonic hypermotility, and (3) ileal stasis. It may be worth while to mention here that all these observations are but the signs of ulceration or infiltration of the wall of the intestine, and not one of them offers explanation concerning the cause, which should be determined in the light of clinical and laboratory evidence.

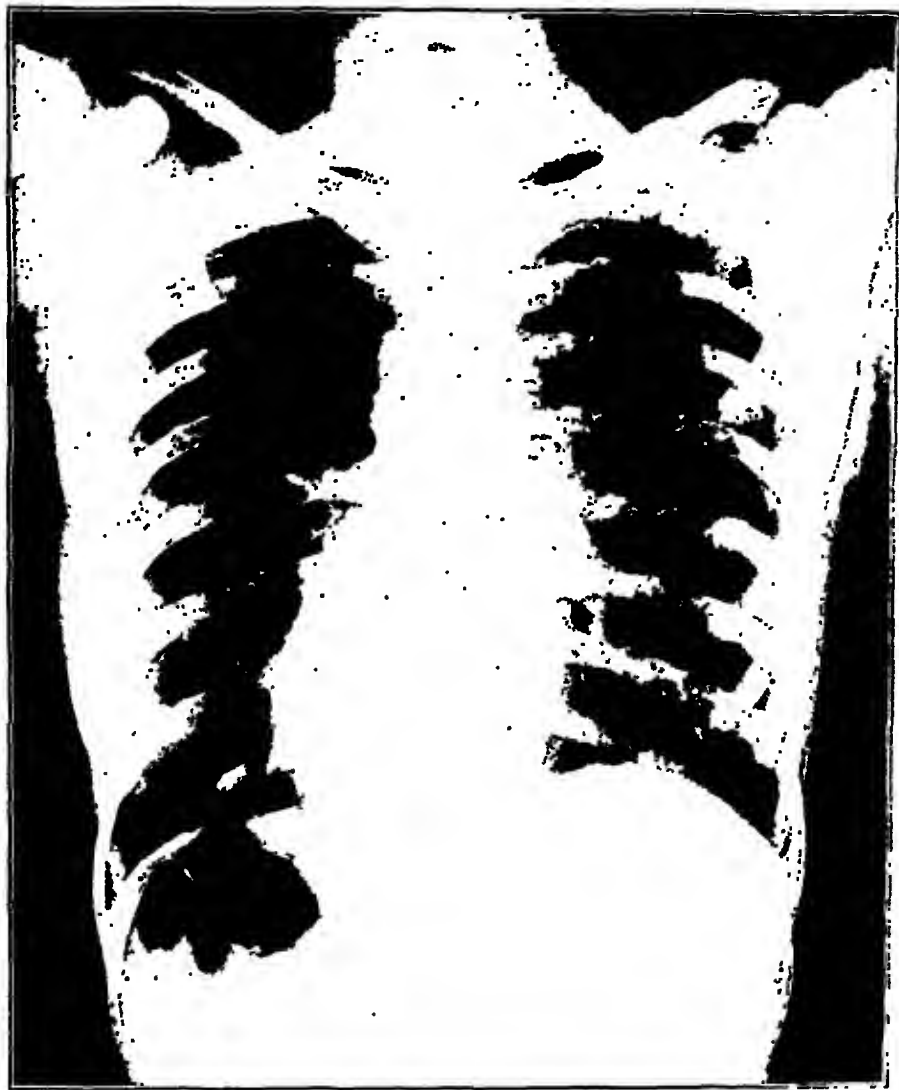


Fig. 7 (case 5).—Roentgenogram of the chest, Nov. 9, 1927, showing fibrotic lesion of lung in first intercostal space area and a calcified mass beneath the third rib near the axilla on the right side. Observations are considered as unimportant.

The greatest amount of information was obtained from examination following both a barium meal and an enema. In one case, the barium enema alone demonstrated the filling defect of the cecum and ascending colon clearly enough for a positive diagnosis to be made. Of the two

# *Data of Patients with Intestinal Tuberculosis with Obstruction*

Case	Age	Sex	Duration of Symptoms	Previous History of Tuberculosis	Nausea and Vomiting	Pain	Leukocytes	Fever	Lungs	Abdominal Examination	Operation	Complications	Pathologic Observations	Results
1	25	M	10 mo.	+	+	++	8,200	0	Latent tuberculosis in both upper lobes	Tenderness and mass in right lower quadrant; no rigidity	Resection of 30 cm. of terminal ileum and cecum; end to side enterocolostomy	Flare up of pulmonary process; superficial infection of incision	Tuberculosis of ileum and cecum, hyperplastic infection with ulceration	Cured
2	30	M	5 yr.	+	+	++	6,400-9,100; polymorphonuclears, 57-70%	0	Latent tuberculosis in both upper lobes; no advancement in 6 years	Tenderness and mass in right lower quadrant; no rigidity	Resection of terminal ileum, cecum and ascending colon; aseptic end to end enterocolostomy prophylactic ileostomy	Slight superficial infection around enterostomy tube	Tuberculosis and schistosomiasis of terminal ileum, cecum and ascending colon	Cured
3	25	F	1½ yr.	None	+	+	4,000-5,300; polymorphonuclears, 68-73%	0	Clear	Tenderness and mass in right lower quadrant; no rigidity; small fecal fistula	Excision of fecal fistula; resection of 30 cm. of terminal ileum, cecum and ascending colon; enterocolostomy; prophylactic ileostomy	Phlebitis of left femoral vein	Tuberculosis of ileum, cecum, appendix and ascending colon	Well enough to go to school but some vague abdominal discomfort
4	11	F	7 mo.	0	+	+	8,100; polymorphonuclears, 71%	39.2 C.	Negative on physical examination; X-ray shows thickening of shadows of the hilum thought to be of some importance	Doughy in consistency, and mass and tenderness in right lower quadrant; no rigidity	Extensive exploratory laparotomy; enterostomy for obstruction	Flare up of pulmonary process; steady decline; intestinal obstruction	No autopsy	Died

## DIAGNOSIS

The two conditions with which one is most likely to confuse these hyperplastic occlusive lesions of the cecum are: appendicitis and malignant growth.

A malignant growth is usually seen in older people; it is most often associated with blood and mucus in the stools, and the symptoms are generally of short duration. My cases were all in young people between 25 and 30 years of age, and a malignant tumor was not probable. During the time in which this series of cases was collected a patient with a malignant growth in the right colon was not encountered.

The difficulty, therefore, has been to exclude appendicitis, and since the first two cases I have been moderately accurate in diagnosis. As already stated, all of my patients were admitted with a provisional diagnosis of appendicitis. If the history and clinical picture aroused suspicion of intestinal tuberculosis, a series of roentgen-ray pictures was made. One must, however, constantly have in mind the danger of this delay if one is dealing with a case of acute appendicitis. Three of my patients subjected to roentgen-ray examination were found to have chronic appendicitis with normal cecums.

If a patient with a suggestive history has a mass in the cecal area, a normal or nearly normal temperature, pulse rate and white blood count, no acute tenderness and no involuntary muscular resistance or rigidity, I have felt safe in carrying on the roentgen-ray studies of the intestine. Hourly counts were made in one case with leukocytosis, and the temperature was closely watched.

In case 8, the clinical diagnosis of intestinal tuberculosis was not confirmed by roentgen-ray studies but was demonstrated at operation: this case was in an early stage; with most of the lesion in the appendix and head of the cecum only. In another case of subsiding appendicitis, the roentgen-ray report indicated a hyperplastic occlusive lesion in the cecum; however, a lesion was not found at operation. With these two exceptions the roentgen-ray studies have not failed to give an accurate idea of the condition.

## TREATMENT

Resection of the diseased portion of the bowel with enteroclostomy is the operation of choice; this was done in six cases, with one death and five recoveries resultant. I have developed an aseptic technic based on the method of Scarff,<sup>10</sup> and adapted it to end to side anastomosis; this has been described and illustrated in detail elsewhere.<sup>11</sup> Sometimes the

10. Scarff, J. E.: Aseptic End and End Suture of Intestine, *Ann. Surg.* 83: 490 (April) 1926.

11. Branch, J. R. B.: Aseptic Intestinal Anastomosis in Resection of the Large Bowel, *Surg. Gynec. Obst.*, 1928.

terminal ileum is as large as the colon, and end to end anastomosis is done. The patient in case 4 had also extensive tuberculous peritonitis and was not in condition to stand more than an enterostomy to relieve obstruction. The patient in case 7 was also in rather poor condition, and there was extensive and massive involvement of the mesenteric and

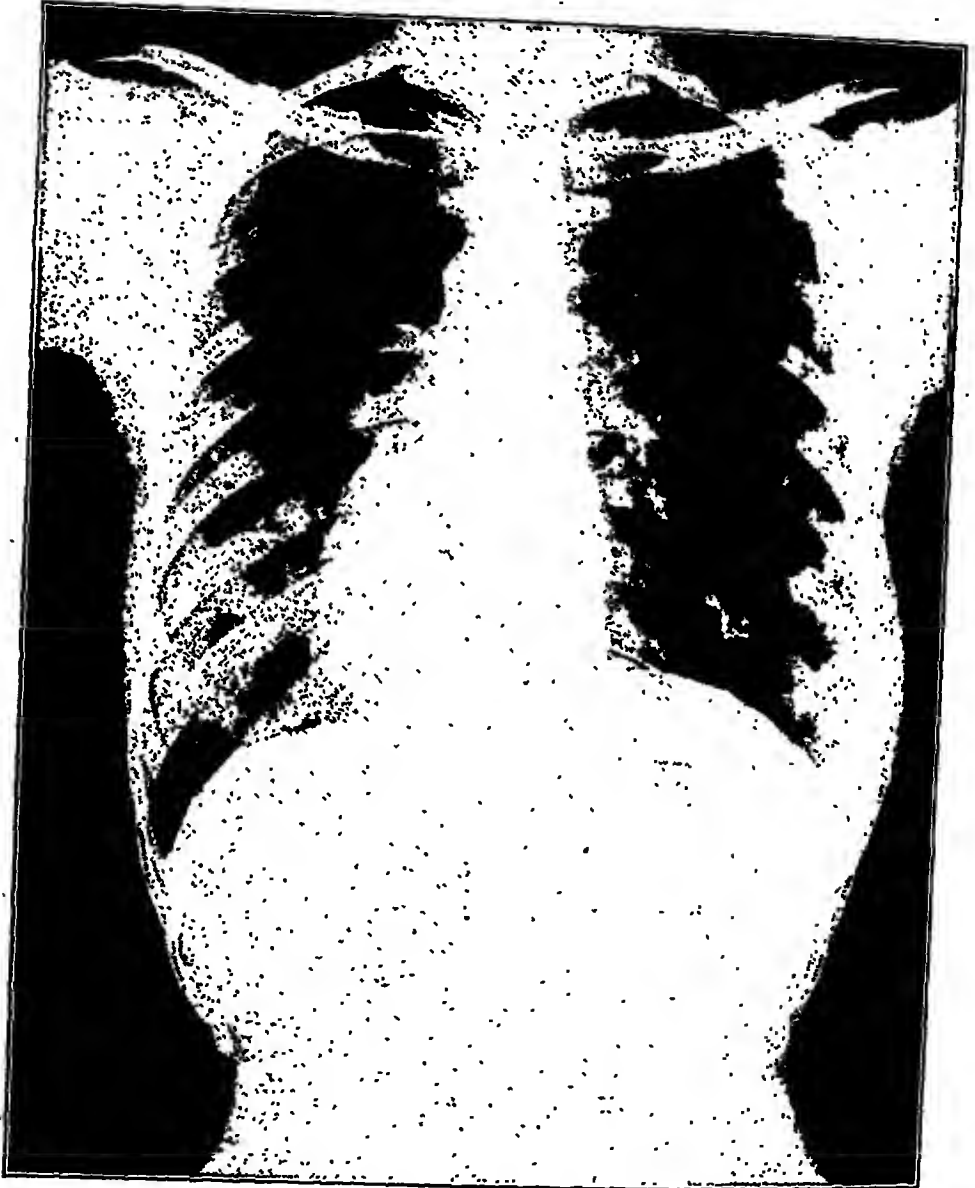


Fig. 9 (case 6).—Roentgenogram of the chest, June 3, 1927, showing normal lungs.

retroperitoneal glands, with caseation and softening; the abdomen, after exploration, was closed, without further treatment. In such a case, the surgeon might consider isolating the diseased portion of the bowel, leaving it in situ, bringing the two cut ends out through the skin, suturing them there and, at the same time, doing an enterocolostomy. When the





ileus and its consequences, and (2) the limiting, for four or five days after operation, of all fluid intake to the subcutaneous and intravenous administration of solutions of physiologic sodium chloride or dextrose. Nothing is given by mouth or rectum, and the liberal use of morphine further helps to reduce peristalsis to a minimum.

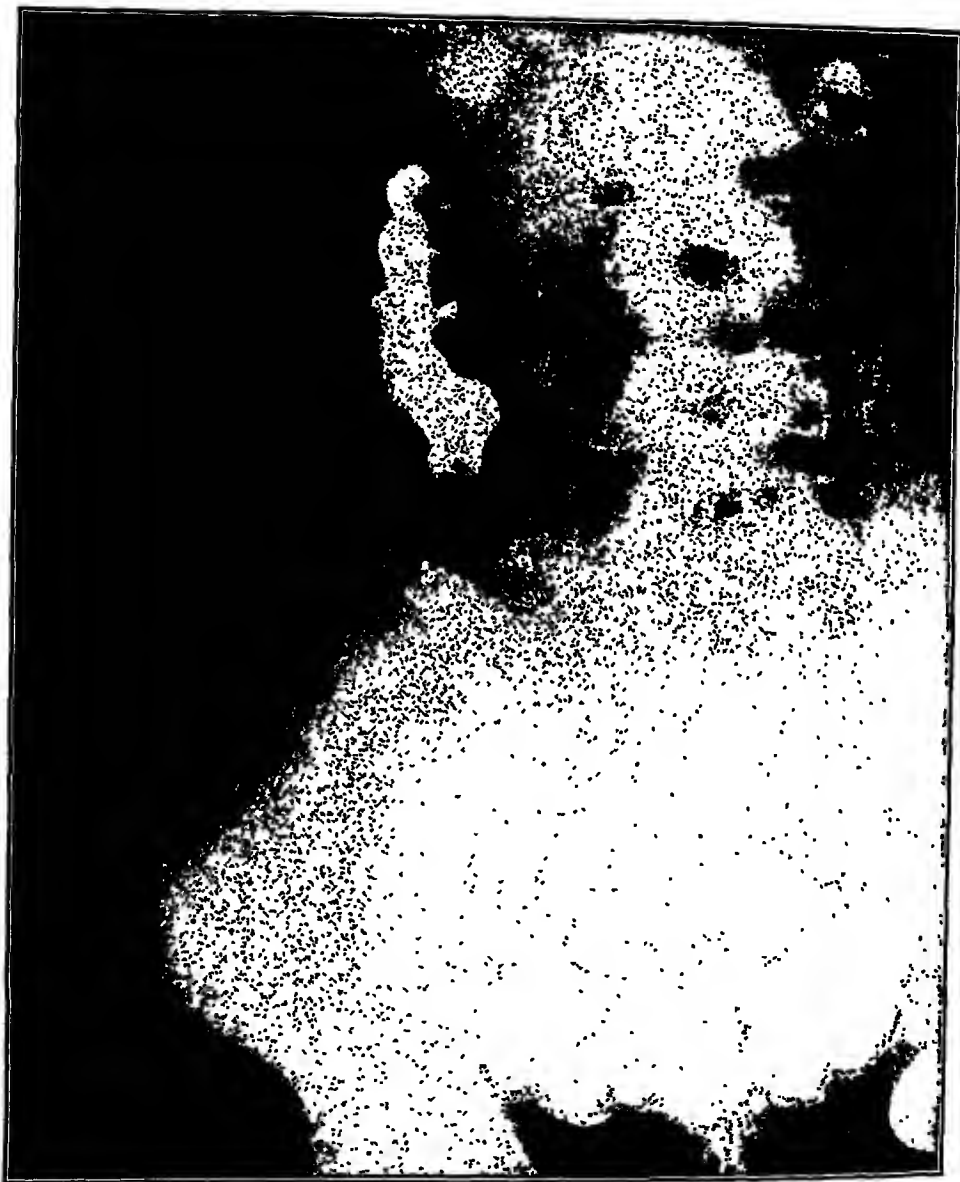


Fig. 11 (case 6).—Roentgenogram, Dec. 7, 1927, made eight hours after ingestion of barium, showing marked ileal stasis. The head of the barium column has reached the descending portion and sigmoid.

#### RESULTS

It is too early to report end-results in any of my cases. In the first five resections, there was no mortality; in the sixth, the patient died of pneumonia and peritonitis. The autopsy showed a leak at the anasto-

patient's condition permits it, this isolated section, by this time merely a mucous tube freed from the fecal current, may be excised. As the obstruction in my case of this type was not extensive, I decided to try general reconstructive treatment with heliotherapy and, later, resection. A simple short circuiting entero-enterostomy has not proved of great



Fig. 10 (case 6).—Roentgenogram, Dec. 6, 1927, made after the injection of a barium enema, showing no filling of the cecum and dilatation of the terminal ileum.

valve. Considerable importance is attached to two features in the operative and postoperative procedure: (1) the prophylactic or complementary enteroenterostomy suggested by Charles Mayo to avoid possible paralytic

gas per rectum spontaneously, and stools were normal when food was given by mouth. The enterocolostomy openings functioned normally in all cases as shown clinically and by follow-up roentgen-ray examinations. One patient died—the patient in case 4, who had extensive intestinal tuberculosis of the early plastic stage in addition to the intestinal lesion. Emergency enterostomy was performed to relieve intestinal obstruction, and the patient died forty-two days after operation. Five patients are well enough to carry on their usual vocations.

mosis with a resultant peritonitis. The area of cecal involvement was slightly greater than estimated at operation, and not enough of the bowel was resected; the sutures, not being taken in healthy normal colon, sloughed; the patient also had pulmonary tuberculosis and bronchopneumonia. In three resections, some local infection was present in the



Fig. 12 (case 5).—Specimen removed at operation, described in text.



Fig. 1 (case 1).—Tumor of the wall of the chest; the area of density is shown extending from the second to the fourth ribs, near the sternal border of the right side.

# MALIGNANT TUMORS OF THE WALL OF THE CHEST

CHARLES D. LOCKWOOD, M.D.

PASADENA, CALIF.

Malignant tumors of the wall of the chest, apart from metastatic carcinoma, are relatively rare. They are usually sarcomatous. Two hundred and thirteen cases were collected by Hedblom<sup>1</sup> in 1921; of these, 61.4 per cent were sarcoma and 18.7 per cent chondroma. Few cases appear in the literature since that time, and in view of the great interest which is now maintained in thoracic surgery, it seems worth while to report two cases in which the patients have been under my care in the past two years.

The pathologic processes of these tumors does not differ from that of sarcoma or chondrosarcoma in other parts of the body. They may take their origin from the soft parts, the cartilage, ribs, sternum, clavicle or scapula. As the growth develops, it invades all of the structures of the wall of the chest and may finally attack the pleura. The two cases here reported began in the cartilaginous portions of the upper ribs near the manubrium.

## REPORT OF CASES

CASE 1.—Mrs. K., aged 50, childless, consulted me in November, 1922, concerning a tumor of the wall of the chest beneath the right breast. She first noticed the tumor in April, 1922. It was painless but seemed to be increasing in size. She had gained in weight. Examination revealed a bony-like tumor involving the third, fourth and fifth ribs on the right side near the costochondral junction. It was slightly movable and not tender. The breast was normal; there were no enlarged axillary glands. Stereoscopic x-ray films showed an area of increased density, 8 by 6 cm. between the first and fourth ribs. There was no involvement of the ribs, and the tumor mass appeared to be anterior to them. No roentgenographic diagnosis was possible.

*First Operation.*—Nov. 28, 1922: The tumor was exposed by a transverse incision just below the clavicle. It proved to be cartilaginous, 6 cm. in diameter, lying between the first and second ribs, extending inward to the pleura and outward between the ribs for 2 cm. There was erosion of the first rib. The tumor was excised down to the ribs and then curetted out as far as seemed safe without penetrating the pleura. One hundred milligrams of radium screened with 2 mm. of brass was left in the cavity for twelve hours.

1. Hedblom: Tumors of the Bony Wall of the Chest. *Ann. Surg.* 3:5 (July) 1921.



Fig. 3 (case 1).—Lateral view of tumor.



Fig. 2 (case 1).—Recurrence of tumor at original site. The area is less dense.





Fig. 5 (case 1).—View of tumor showing denser shadow but without apparent extension.



Fig. 4 (case 1).—Greatly increased area of density extending outward to lateral border of the chest.

*Second Operation.*—July 21, 1924: The old scar was excised and the incision enlarged. The tumor had recurred at the original site. The first rib was eroded and destroyed for 2 or 3 cm. outward from its sternal junction. There were two or three recurrent nodules in the periosteum overlying the second rib. The second rib was removed for 2 inches (5 cm.), the first rib and sternum thoroughly curetted. The pleura was accidentally opened but no serious symptoms followed. Fifty milligrams of radium in bare needles were inserted into the area of the tumor. The radium was left in ten hours. The patient remained well until May 20, 1927, when she returned complaining of pain in the right arm and some restriction of motion. The tumor had recurred in the scar in the second rib farther out and beneath the clavicle. X-ray examination showed involvement of the second, third and fourth ribs.

*Third Operation.*—June 13, 1927: A large flap was made by a curved incision beneath the breast and pectoral muscles. The second, third and fourth ribs were



Fig. 7 (case 1).—Scar from operation; the right breast is slightly elevated.

divided at the sternocostal junction and the pleura opened to inspect the tumor. It had involved the third rib in the anterior axillary line and there was an extension within the chest cavity involving the second, third and fourth ribs and the parietal pleura. A tumor mass 5 or 6 inches (12.7 or 15.24 cm.) in diameter projected into the pleural cavity and was attached to the upper lobe of the lung. The tumor masses involving the ribs were all curetted and 50 mg. of radium in 12.5 mg. bare needles was inserted into the tumor mass within the chest cavity and left in twenty-four hours. The defect in the wall of the chest was closed by sliding up the breast and pectoral muscles. The wound healed without infection.

*Present Condition.*—Feb. 10, 1928: Clinically, this patient has remained well, but a recent examination revealed a tumor mass 2 cm. in diameter between the axillary folds, firmly attached to the wall of the chest. X-ray films do not show any increase in the size of the tumor within the chest cavity.

*Pathologic Process.*—Grossly, this tumor consisted of pearl-like cysts which formed pockets in the cartilage of the ribs and later invaded the bony portions of the ribs and manubrium.



Fig. 6 (case 1).—Lateral view of tumor showing invasion of pleura and lung.

The microscopic report was made by Dr. A. M. Moody. The tissue consisted essentially of hyaline cartilage with many nuclei, having the appearance of dividing cells and some round cells. As a whole, it presented the picture of a malignant growth. A diagnosis of chondrosarcoma was made (figs. 1 to 8).

CASE 2.—A man, aged 26, a concrete worker, for one month prior to my first examination had noticed a swelling in the region of the right pectoral muscle just below the clavicle. Six years before, he was struck on the chest with a piece of iron, near the site of the present tumor. The scar of this injury is still visible. He was otherwise healthy. The results of the examination were negative except for the presence of a semifluctuating tumor, 6 cm. in diameter lying just beneath the right clavicle and extending from the outer border of the sternum to a line drawn from the central portion of the clavicle. The tumor was painless, some-

#### DATA IN CASE 2

200 Kilovolts, 4 Milliamperes, 50 Cm. Distance, 18 Cm. Aperture,  $\frac{1}{2}$  Mm. Copper, 1 Mm. Aluminum Filter

12/15/26	Upper anterior right side of chest.....	15 minutes
12/16/26	Upper anterior right side of chest.....	15 minutes
12/17/26	Upper anterior right side of chest.....	20 minutes
12/20/26	Upper anterior right side of chest.....	20 minutes
12/22/26	Upper anterior right side of chest.....	20 minutes
12/24/26	Upper anterior right side of chest.....	20 minutes
12/27/26	Upper anterior right side of chest.....	10 minutes
12/27/26	Right posterior angle of scapula.....	10 minutes
12/29/26	Right posterior angle of scapula.....	20 minutes
1/ 3/27	Right posterior angle of scapula.....	20 minutes
1/ 5/27	Right posterior angle of scapula.....	20 minutes
1/ 8/27	Right posterior angle of scapula.....	30 minutes
1/10/27	Right posterior angle of scapula.....	20 minutes

Pain diminished; mass in back became smaller; open wound in anterior aspect of chest cleaner

2/ 8/27	Right anterior side of chest.....	30 minutes
2/ 9/27	Right anterior side of chest.....	30 minutes
2/11/27	Right anterior side of chest.....	30 minutes
2/12/27	Right posterior side of chest.....	30 minutes
2/18/27	Right posterior side of chest.....	30 minutes

Following first treatments pain ceased; general condition improved; wound in anterior chest wall closed in considerably; remaining area shows clean granulations.

what movable and apparently attached to the underlying structures. X-ray films revealed an area of only slightly increased density at the site of the tumor.

**Operation.**—July 29, 1926: A curved incision over the wall of the chest exposed a tumor, 6 cm. in its long diameter, densely adherent to the third rib and involving its periosteum. The tumor was vascular and had infiltrated the pectoral muscles and passed between the third and fourth ribs, involving the parietal pleura. The tumor was excised as widely as possible; 50 mg. of radium screened with 2 mm. of brass was left in the wound for twelve hours. The wound did not heal readily. There was a free discharge of cheesy material and free hemorrhage. In September, 1926, 50 mg. of radium was placed in the cavity in bare needles for two hours. The wound improved much after this and granulations assumed a healthy appearance, but a pocket still persisted which continued to discharge and bleed.

Nov. 8, 1926: Four months after operation, 1,200 mg. hours of radium in bare needles were given in different portions of the tumor. There was a well marked constitutional reaction and the tumor shrank greatly. However, it continued to bleed freely and at each dressing fragments of grayish necrotic material escaped. At this time, a tumor appeared near the angle of the right scapula

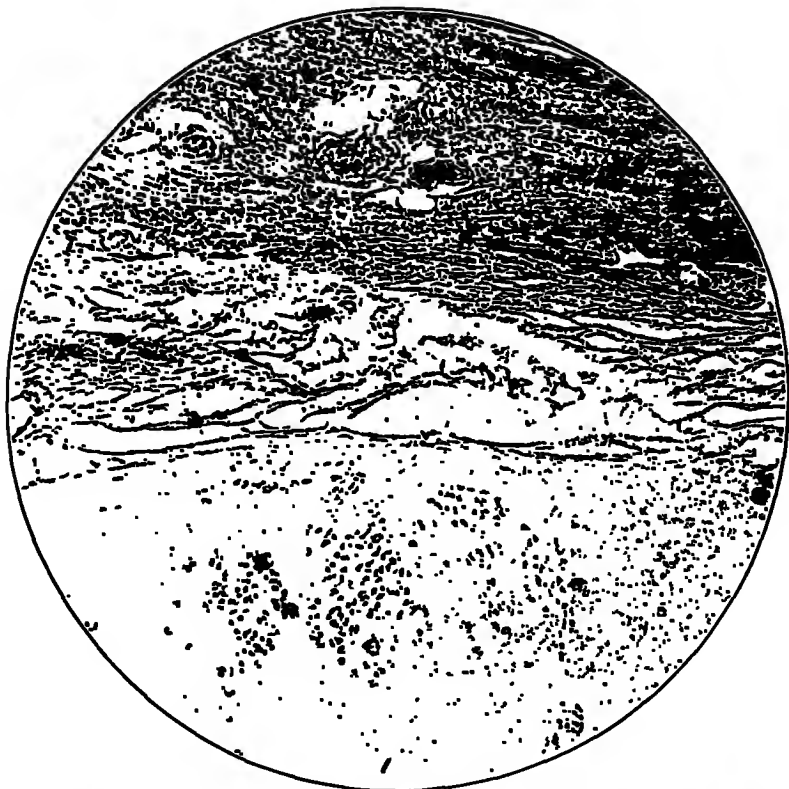


Fig. 8 (case 1).—Tumor of the wall of the chest; chondrosarcoma;  $\times 75$

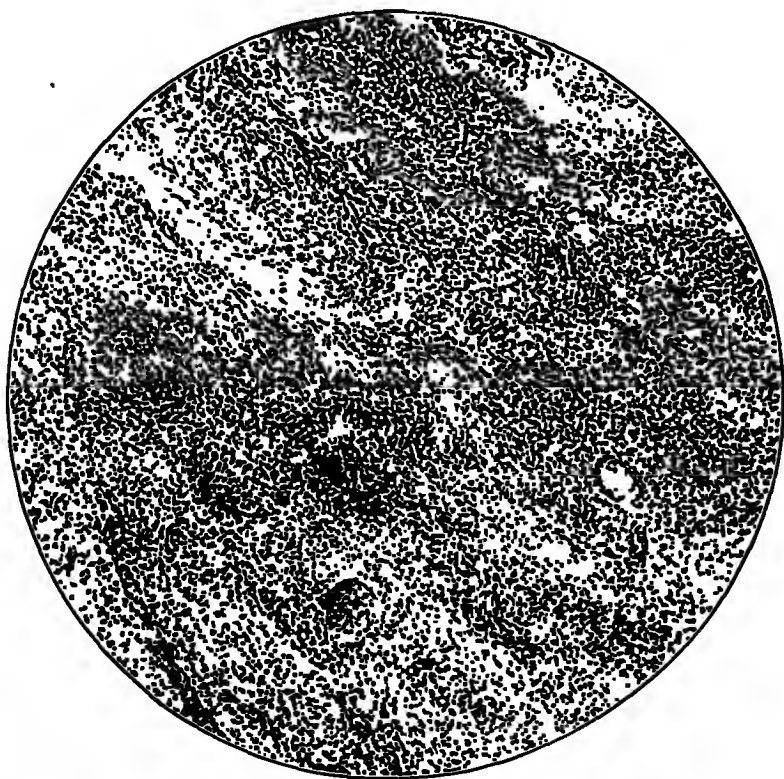


Fig. 9 (case 2).—Tumor of the wall of the chest; round cell sarcoma;  $\times 75$ .



Fig. 12 (case 2).—Sarcoma of the wall of the chest.



Fig. 13 (case 2).—Metastatic sarcoma of the back.



Fig. 10 (case 2).—Same as figure 9, showing more detailed structure;  $\times 300$ .



Fig. 11 (case 2).—Infiltration of the muscle fibers;  $\times 100$ .



# CRANIOTOMY INCISIONS WITHOUT FORCEPS\*

ALBERT S. CRAWFORD, M.D.

DETROIT

The control of hemorrhage is one of the most important and yet difficult problems in all extensive craniotomies. The tourniquet, hemostatic stitch and pedicle clamp have been replaced largely by the multiple forceps method now commonly used. The covering of the scalp is generally accomplished by towels clamped or sewed to the cut edges.

During the past two years, my co-workers and I have been using a method which keeps the operative field free of forceps and which at the same time efficiently covers the scalp, controls bleeding and protects the edges of the incision. This is by the use of stockinet and Michel clips.

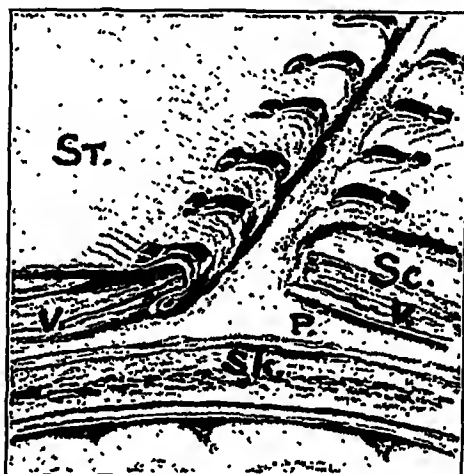


Fig. 1.—Placement of Michel clips on skin incisions. *ST*, indicates the stockinet covering; *Sc*, the scalp; *V*, the vein; *P*, the pericranial layer and *Sk*, the skull.

We experimented on various metal clips, but finally settled on the Michel type, for they are already available, are inexpensive, are easily applied and control hemorrhage efficiently.

A few points in the technic might be mentioned. After the field block has been made with procaine hydrochloride, the incision line is scratched till it bleeds, then the stockinet is laid over the whole operative field and cut along the blood-stained line. The skin incision is made in the usual manner, a few inches at a time, and bleeding is controlled by digital pressure. When a spurting vessel is encountered, it is caught at once and stick tied with silk. All other oozing is controlled with the clips. Figure 1 shows how the clips are placed, external to the

\*From the Henry Ford Hospital.

which was similar in appearance and consistency to the original tumor. The patient was now referred to the x-ray department for deep therapy. He was given treatments to the point of tolerance. He had a severe reaction from the x-ray therapy. There was marked improvement in the original tumor with diminished discharge and less hemorrhage. The tumor on the back almost disappeared.

*Pathologic Process.*—Grossly, this tumor consisted of grayish white tissue. It was soft, friable and seemed to infiltrate the muscle. There was no regular form or contour. In places, it seemed glandular (fig. 9 to 13).

Microscopically, it consisted of small round cells, infiltrating the adjacent muscle fibers. A diagnosis of round cell sarcoma was made.

*Present Condition.*—Feb. 10, 1928: The patient has lost 10 pounds (4.5 Kg.) in weight; he is anemic and weak. The tumor has not increased in size but it is still discharging, bleeds freely and has eroded the second rib. There is a dense fibrosis of the pectoral muscles, and he is unable to abduct his arm or lift it above his head. The tumor over the scapula has not recurred, but there is an ulcer 2 cm. in diameter at its former site. No metastasis can be discovered either by examination or on the x-ray films.

#### COMMENT

Tumors of the wall of the chest are usually malignant. The most common forms are sarcoma and chondrosarcoma. These tumors usually recur after removal. The patients are best treated by thorough removal, radium and x-ray therapy.

Unfavorable results have not followed this method so far. Some sloughing of the skin edges occurred in one case, resulting in delayed union, but this was attributed to extremely low blood pressure following the operation and to probable thrombosis of the vessels. The clips, of course, may have been contributing factors. This danger from pressure should be kept in mind.

Essentially the same method was recently described for incisions on the extremities by Dr. W. E. Johnston.<sup>1</sup> We agree with him that the method can be effectively used for protection of wounds in all surgical incisions, except probably those leading to large cavities, such as in laparotomies, in which clips might be dislodged and lost. A refinement in technic might be elaborated by having the clips all fastened to a string or wire, which would eliminate the danger of any being lost.

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1. Johnston, W. E.: Method of Operative Protection from Skin Infection, *J. A. M. A.* 88:1320 (April 23) 1927.

pericranial layer, about 12 mm. apart and directly over bleeding points wherever possible. Figure 2 shows a temporoparietal incision all ready for the work on the skull, and figure 3 the clips, the holder and the forceps used.



Fig. 2.—Temporoparietal incision with clips already placed.



Fig. 3.—Michel clips (small size) single (top and side views), on the wire holder, and one in the forceps which is used to apply (reduced one-half).

After the bone flap has been turned, the wound edges are covered with wet cottonoid sheets, so that the field is smooth and level and the clips are protected. During closure, the clips are removed a few at a time, as the skin sutures are placed and tied, to prevent excessive bleeding from the scalp.

sciousness and an x-ray picture is made, it is found, however, that the reestablished muscle spasm has again pulled the fragments out of alinement. The remedy is manifestly to be found in traction or extension to avail of not only marshaling the fragments by the encircling soft parts, but to overcome muscle spasm before final fixation. In such cases, the traction should be continued until the muscle spasm ceases. Fractures at the middle of the forearm, after reduction with immediate fixation, are most prone to get out of alinement from the continuance of muscle spasm of the pronators, with an ultimate lessening of the interosseous space and rotatory movements of the forearm, unless corrected early.

Economy in x-ray pictures, after reduction of fractures and prior to good callus formation, is false economy, and the relation of the fragments to each other should be frequently determined, not presupposed, especially in the early stages of healing.

In order to emphasize the points that I desire to bring out in this paper, it may be well to recapitulate certain points concerning aids in restitution which should be considered.

1. Traction on the surrounding encircling soft parts should be utilized to help assemble the fragments, in addition to any manipulation or leverage that the surgeon can effect from without.

2. The possibility of postanesthetic muscle spasm pulling the fragments out of alinement must be borne in mind. In suitable cases, it will be well to use traction until muscle spasm is permanently overcome.

3. Fixation should be used only after muscle spasm is overcome in cases in which muscle spasm can distort the parts.

4. X-ray pictures should frequently be made until callus formation assures the desired restoration. The surgeon should not be content with an x-ray picture before the cast or splint is applied and after it is taken off.

#### REPORT OF A CASE

In order to illustrate the foregoing principles, the following case will be cited as being typical.

H. C., aged 28, fell off a platform about 8 feet high (244 cm.) on June 27, 1926, striking on his left shoulder. A report of his condition at that time states that pain and crepitation were present. A depression was noted under the left acromion process, and there was undue fulness on the anterior aspect of the joint. The arm was rotated inward and abducted, and the forearm was supported by the right hand, near the elbow.

An x-ray picture made at that time showed a fracture dislocation at the proximal end of the left humerus. The dislocation was of the subcoracoid type, being anterior and inward from its proper position, so that the glenoid was not visible in the roentgenogram. The fracture was of the surgical neck, and from the

# FRACTURE DISLOCATION OF THE SHOULDER

## RELATION OF SOFT PARTS TO RESTORATION: A NEW METHOD OF TREATMENT

R. TUNSTALL TAYLOR, M.D.

Professor of Orthopedic Surgery, University of Maryland

BALTIMORE

As a general rule, a fracture or dislocation is thought of by the general practitioner solely in terms of the relation that bones or fragments of bones bear to each other. The effect of the soft parts in restoring normal alinement or in preventing it is lost sight of.

The interposition of soft parts in preventing union, causing malunion or interfering with restitution is well recognized and will not be discussed. But the clinician with increasing experience is more and more impressed with the importance of the utilization of the closely encircling muscles, ligaments, tendons, capsule and periosteum or portions of the latter in marshaling fragments into alinement. Failure to consider this important factor often leads to poor end-results, disappointment to the attendant or serious disability to the patient.

In such complicated joints as those of the shoulders and hips, this is especially important, and a precise knowledge of the anatomy of the parts, the exact function of each muscle and the direction of the forces that produced the disability should be known.

In the treatment of patients with intracapsular fracture of the hip, Royal Whitman of New York places the patient in the now well recognized "Whitman position," and by extreme abduction makes use of the capsule put on the stretch to marshal the fragments into apposition. This is aided through fixation of the pelvis by abduction of the other leg and by traction and inward rotation of the affected one. In this connection, Lovett and Jones<sup>1</sup> say that "any treatment which ignores the fundamental principles of abduction, extension and internal rotation in intracapsular fracture of the hip, should be ruthlessly condemned as obsolete," but they fail to explain the *modus operandi* of the soft parts.

During the early stages of fractures and dislocations, muscle spasm is known to play an important rôle in preventing reposition, but its continuance after reduction is frequently overlooked. Thus, with the patient under an anesthetic, a fracture is reduced and the part involved placed in a carefully applied plaster cast, and the surgeon has a comfortable feeling that all is well. When the patient regains con-

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1. Lovett and Jones: Orthopaedic Surgery, New York, William Wood & Company, 1923, p. 404.



Fig. 2.—Fracture-dislocation in plaster cast after attempt at manipulative reduction.

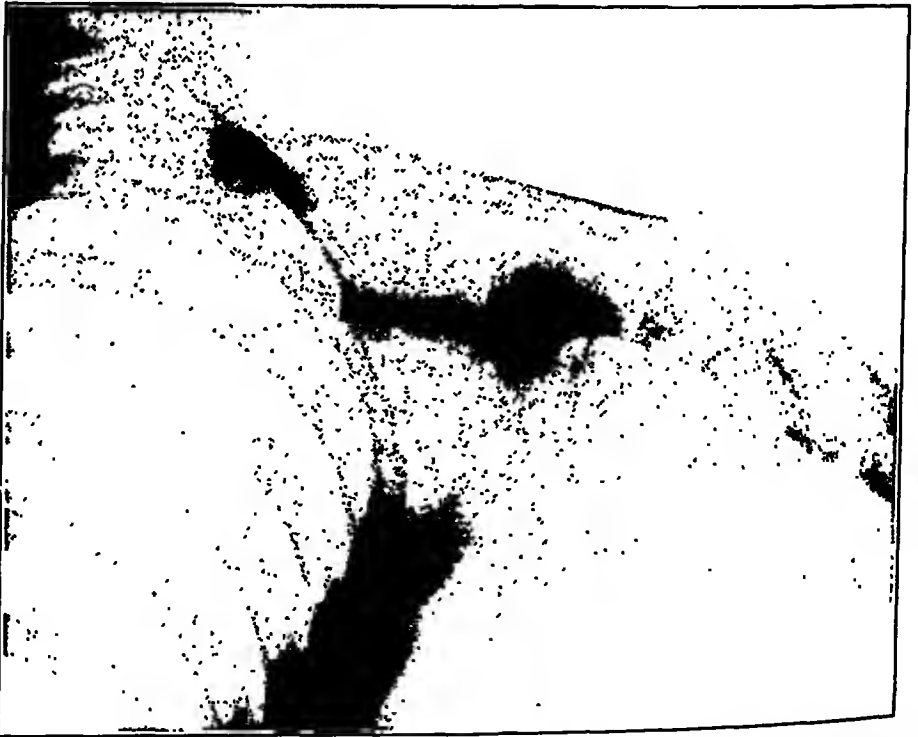


Fig. 3.—Forty-eight hours after traction (15 pounds) on distal fragment and suspension of 5 pounds each of the forearm and humerus to separate pulleys. Abduction of humerus 60 degrees. Dislocation reduced.

muscle spasm of the supraspinati and infraspinati the proximal fragment or humeral head had rotated through an arc of 180 degrees, so that its fractured surface was directed upward; the line of fracture of the distal end was horizontal and slightly below and external to the articular surface of the fractured humeral head (fig. 1).

Prior to the time the patient entered my service, an attempt had been made to reduce the fracture and dislocation while he was under an anesthetic, with the result that the distal fragment had slipped into the axilla and was abducted at an angle of 45 degrees with the body and was causing much axillary pain from impingement on nerves. The proximal end or head was unchanged in position. After this manipulation, it was held in position by a plaster cast covering the arm

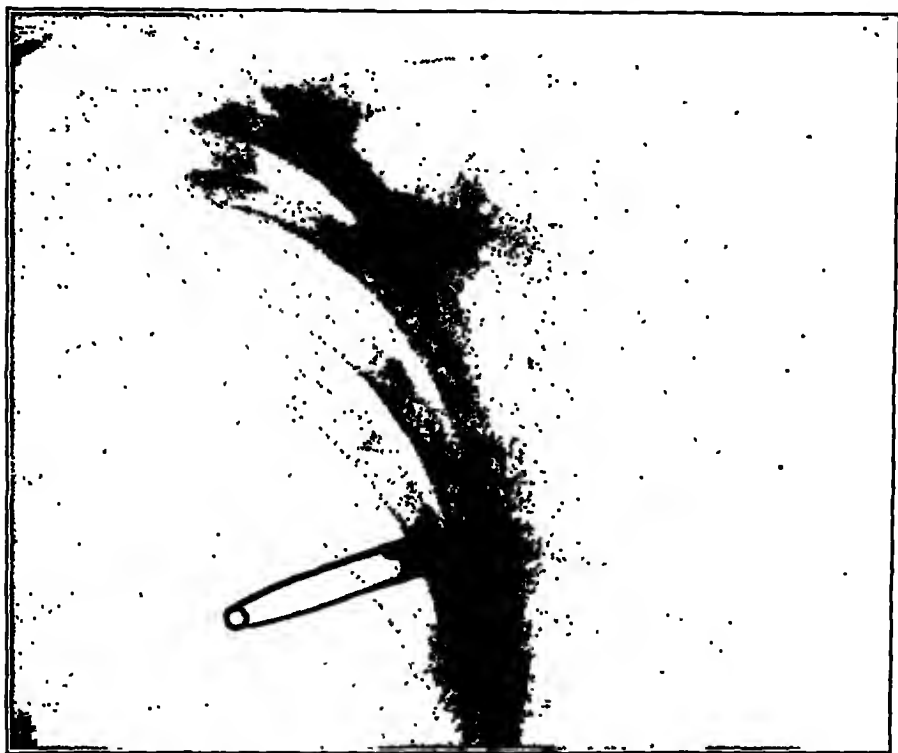


Fig. 1.—Fracture-dislocation of left shoulder immediately after accident.

and thorax (fig. 2). The patient was referred to me in this condition seven days after the accident, and was admitted to the hospital on July 2, 1926.

For this condition, various manipulative procedures of doubtful value have been suggested and tried, with the patient under general anesthesia; also similarly ineffective open-operative methods of grafting, suture, screwing the parts together, bone-pegging and even removal of the dislocated proximal fractured head. In these cases, it is wisest to put into practice the principles set forth in the first part of this paper. As in the present case neither the dislocation nor the fracture had been reduced by manipulation, the retaining cast was removed and the patient put up in a Balkan frame. He was placed flat on his back with the spring and mattress made additionally firm by cross-slats. Projecting from under the mattress beyond the left side of the bed for about 2 or 3 feet (61 or 91 cm.) was a board 5 feet (152 cm.) long and 4 inches (10 cm.) wide; to its upper surface at the



sion of the forearm and of the arm, and in abduction at the side of the bed, from 10 to 15 pounds (4.5 to 6.8 Kg.) were used as the case progressed (figs. 3 and 4).

This apparatus was applied on July 2, and on July 6, the x-ray picture showed that reduction of the dislocation had been effected (fig. 5). Abduction of the arm at this time was about 45 degrees with the body, and it was seen that the apposition of the fragments was not in good alinement. It was therefore increased to 60 degrees and later to 90 and 120 degrees until perfect alinement was obtained (figs. 5, 6 and 7).

On July 28, after three weeks of treatment in bed, when the x-ray examinations showed good callus and a reduction of the dislocation and normal alinement at the fracture, the arm was carefully held in the position maintained by the



Fig. 6.—Abduction of humerus 90 degrees.

Balkan frame apparatus, the patient slowly assisted into a sitting position in the bed, and a plaster cast applied from the left hand to below the crests of the ilia (fig. 8).

This position was approximately with the humerus abducted 120 degrees with the body, rotated outward 60 degrees and the forearm flexed 90 degrees.

The cast was bivalved horizontally on August 19, so that the upper portion could be removed to permit massage and passive upward and anteroposterior motions. On September 2, the cast was removed, a cravat sling used and passive and active motions permitted to allow full function, which soon followed.

In approximately ten weeks following a fracture dislocation, this man was back on the job with full restoration of function.

The method used has proved satisfactory in this and similar cases. It substantiates the claim made that the soft parts may aid materially

outer end a similar piece of board, about 4 by 4 inches was nailed at right angles; at its center it was surmounted by a vertical pulley, which was screwed in. By means of this rough board, which the mattress and the patient's weight held in any position in which it might be placed by the surgeon, horizontal traction over the pulley could be made at any desired angle of abduction by means



Fig. 4.—Position of patient in Balkan frame.

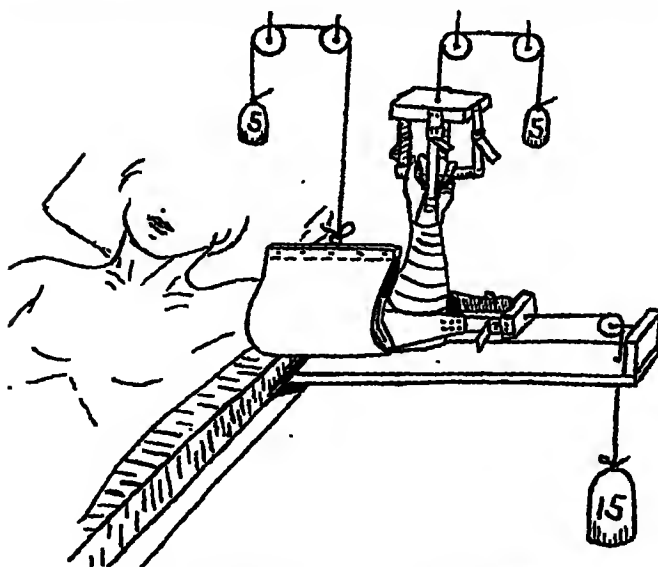


Fig. 5.—Diagrammatic drawing of apparatus.

of adhesive straps and a spreader attached to the upper arm. The forearm, by means of adhesive traction straps from elbow to hand, and the upperarm, supported by a sling with spreader, were suspended from the overhead bars of the Balkan frame, with appropriate pulleys and counter-balance weights. These enabled the patient to change his position within reasonable limits and facilitated nursing. About 5 pounds (2.3 Kg.) each were used as counterpoises for suspen-

in reducing dislocation and getting the parts of fractures in line when by properly directed traction muscle spasm is overcome.

I claim, therefore, that traction in abduction and outward rotation, putting the capsule on the stretch, in early treatment will reduce anterior and inward dislocation of the humeral head and that hyperabduction, carefully guided by a series of x-ray studies, may entirely overcome the nonalignment in this most disabling condition.

In contrast, it may be well to review briefly comments in leading textbooks on the prognosis and treatment of this serious injury.

C. L. Scudder,<sup>2</sup> speaking of fractures, epiphyseal separations and dislocations of the humeral head, says:

"An anaesthetic must be used for examination and diagnosis, but it is even more important, however, that the first retentive dressing be applied with the assistance of an anaesthetic. Traction, counter traction and manipulation will secure coaptation of the fragments. To hold these fragments securely is difficult—to hold any one of these fractures without operative interference may be impossible." He recommends after reduction, a V-shaped axillary pad, coaptation splints, a plaster shoulder-cap and arm and body plaster of paris or crinoline, with arm at the side and forearm across abdomen, thus rotating the lower fragment inward, the malposition of fracture in this region. Further on, he says that "if traction on the humerus and pressure on the loose head in the axilla fails, open incision is to be done, using the McBurney-Porter hook on the upper fragment and if successful, suturing the shaft with absorbable suture or fine silver wire. . . . If it is impossible to reduce the dislocated head or if it is much comminuted, it will be necessary to excise it."

Sir Robert Jones<sup>3</sup> says:

"The upper fragment formed by the articular head is liable to be rotated into any position and dislocated from the glenoid surface . . . A rotated or dislocated intra-articular fragment will very probably require reposition by operation; this is easily done by the anterior deltoid incision, but there is some liability to recurrence of displacement. If this recurrent displacement cannot be prevented by one or two screws driven through the tuberosity, the head of the bone ought to be removed, but resection more extensive than this is to be avoided."

He also recommends the axillary pad to prevent the adduction of the upper end of the lower fragment, and in closed reductions, he straps the inward rotated arm to the body.

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2. Scudder, C. L.: *Treatment of Fractures*, ed. 3, Philadelphia, W. B. Saunders Company.

3. Jones, Robert: *Orthopaedic Surgery of Injuries*, London, Oxford University Press, 1921.

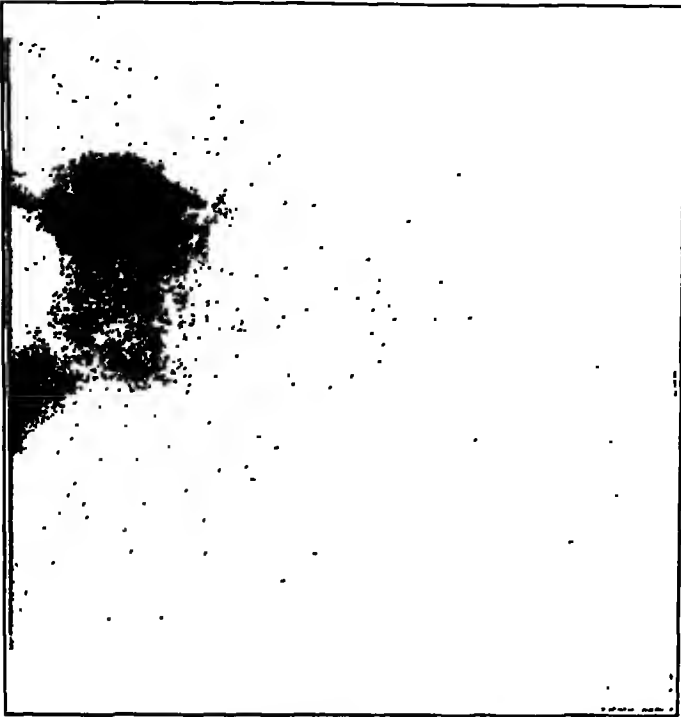


Fig. 7.—Abduction of humerus about 120 degrees. Fracture reduced and perfect alinement. Note intact periosteum between fragments seen below.



Fig. 8.—Patient shown in plaster cast shortly after application in same position as that maintained in the Balkan frame.

# WOUNDS OF THE HEART

## REPORT OF TWO CASES \*

D. M. COX, M.D.

LOUISVILLE, KY.

Of penetrating wounds of the thorax, those involving the heart are relatively infrequent. During the past four years, there have been thirty-five cases of gunshot wounds and sixty-one of stab wounds of the chest at the Louisville City Hospital. Only one bullet and one knife encountered the heart; some of the other wounds were very near, striking the pericardium, but none of the patients gave symptoms to warrant operative intervention.

Early history contains records of many cases of injuries to the heart, and in each instance the patient died. Aristotle and Galen believed that heart wounds were always fatal. Hollerius<sup>1</sup> (1498-1562) was the first to oppose this idea; he thought that small wounds which did not bleed excessively could heal. The first authentic record of a healed wound of the heart was by Iodinis Wolf<sup>2</sup> in 1642. He found a scar in the heart of a deer, and believed that the animal had received the wound previously and had recovered. In 1761, Morgagni<sup>3</sup> was of the opinion that a rapid collection of blood in the pericardial cavity could compress the heart and stop its action.

In 1868, Georg Fischer<sup>4</sup> collected from the literature a series of 452 cases of wounds of the heart with a mortality of 90 per cent. The treatment employed at that time was rest, venesection, application of leaches and occasionally, when possible, the passage of a catheter or sound into the wound for evacuation of fluid from the pericardial cavity.

In 1881, Roberts<sup>5</sup> suggested that wounds of the heart might be sutured. Suture of the heart muscle was first performed experimentally on rabbits by Black<sup>6</sup> in 1882. The idea met with much opposition—

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\*From the Department of Surgery, University of Louisville School of Medicine.

1. Hollerius, J.: *Communis aphorismi allegati*, quoted from Beck: *Wounds of the Heart*, Arch. Surg. 13:205 (Aug.) 1926.

2. Wolf, Idonis, quoted from Beck.

3. Morgagni, J. B.: *De Sedibus et Causis Morborum*, Lipsiae, sumptibus Leopoldi Vossii, 1829; quoted from Beck.

4. Fischer, Georg: *Die Wunden des Herzens und des Herzbeutels*, Arch. f. klin. Chir. 9:571, 1868; quoted from Beck.

5. Roberts, J. B.: *The Surgery of the Pericardium*, Am. Anat. & Surg. 4: 247, 1881.

6. Black: *Verhandlungen der deutschen Gesellschaft für Chirurgie*, Elften Congress, Berlin, 1882, part 1, p. 108; quoted from Beck.

According to Jones and Lovett: <sup>4</sup>

"This accident (fracture-dislocation) is very crippling and if all trials at reduction fail, an open operation should be performed and the head reduced, an ivory or bone peg being used, if it is found necessary." The Jones rectangular arm splint is then described. Later they say: "If the fracture is at the surgical neck and the head is dislocated, an open reduction should be effected and a plate or graft used . . . . After all operations for reducing fracture and fracture-dislocation about the shoulder, except for fractures in or near the glenoid cavity, the arm should be kept in the abducted plane." This does not coincide with Jones' recommendation of closed reduction.

F. J. Cotton <sup>5</sup> says:

"Fracture of the surgical neck complicating dislocation does occur and is a most formidable complication . . . . Obviously all our methods of reduction are of little use in this condition; it is possible that enough connection of fragments may be retained to permit of reduction by right angled traction with outward pressure on the head. If such attempt at reduction does not succeed, as it usually does not, there is nothing for it but to operate."

#### CONCLUSIONS

The temptation is great to avail oneself of the open operative treatment for fractures whereby one can see exactly what is the situation inside and act accordingly.

Here, however, is a condition wherein utilization of the soft parts and not cutting or further traumatization is indicated. They should be used as tractors to overcome dislocation, muscle spasm and non-alinement of fragments at the shoulder joint.

On account of some of the mutilated and impaired functional results seen after manipulative and operative treatment of fracture dislocation of the shoulder, I feel that the method herein advocated should and can be standardized. Further, probably with the exception of the aid of the x-ray, it can be applied in rural communities far away from great medical centers and hospitals.

207-208 Medical Arts Building.

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4. Jones and Lovett: *Orthopaedic Surgery*, New York, William Wood & Co., 1923, p. 413.

5. Cotton, F. J.: *Dislocations and Joint Fractures*, Philadelphia. W. B. Saunders Company, 1924, p. 211.

heart and may be used without entering either pleural cavity; however, in most injuries the pleural cavity has already been penetrated.

After the heart has been exposed, there are several methods by which the wound may be found and repaired: 1. The heart may be grasped tightly and forcibly pulled out of the wound, where gradual relaxation will reveal the injury, which can then be sutured. 2. The first impulse would be to plug the bleeding area with the finger. This is difficult to carry out, because the beating organ keeps moving out of the way of the finger. If sufficient pressure is exerted to control the bleeding, the friable muscle is apt to be torn and increase the size of the wound. 3. In 1907, Sauerbruch<sup>10</sup> described a method by which the bleeding could be controlled: The middle finger of the left hand is inserted through the great transverse sinus which is situated below the aorta and pulmonary arteries and above all the veins entering the heart. The fourth and fifth fingers are placed below the veins; the latter can be compressed by bringing the third and fourth fingers closer together, and thus keep all blood from entering the heart. The index finger and thumb are left free to steady the heart while the wound is sutured. This pressure cannot be maintained indefinitely, for the heart tolerates ischemia for only a limited period of time. This period of safety has been worked out on animals and varies from  $1\frac{1}{2}$  minutes<sup>8</sup> in the dog to  $3\frac{3}{4}$  minutes<sup>11</sup> in the rabbit. To prolong the ischemia beyond this period of time causes the heart to lose its normal rhythm, which it never regains, or there is subsequent degeneration of the cortical cells. 4. A much simpler procedure was recently developed by Beck and Cutler<sup>12</sup> in doing some experimental work on a method for the surgical relief of mitral stenosis. This method will be given in detail in the first case report.

#### REPORT OF CASES

CASE 1.—M. P., aged 26 (?), was admitted to Louisville City Hospital at 11 a. m. on Oct. 14, 1926. He had received a gunshot wound in the chest a few minutes before admission, the bullet entering just to the left of the sternum in the fifth intercostal space. There was pain only at the site of injury. Examination did not reveal any pathologic process of the lungs; the heart was normal in size, but the sounds were faint; the pulse was weak, with a rate of 84.

Fluoroscopy was performed. The field of the right lung was slightly hazier than that of the left, but there was no conclusive evidence of fluid or pneumo-

10. Sauerbruch, F.: Die Verwendbarkeit des Unterdruckverfahrens bei der Herzchirurgie, *Arch. f. klin. Chir.* 83:537, 1907; quoted from Beck.

11. Laewen, A., and Sievers, R.: Experimentelle untersuchungen über die chirurgisch wichtigen Abklemmungen des grossen gefässs in der Nähe des Herzens unter besonderer Berücksichtigung des Verhältnisse bei der Lungen embolie operation nach Trendelenberg, *Deutsche Ztschr. f. Chir.* 94:5, 1908; quoted from Beck.

12. Beck, C. S., and Cutler, E. C.: A Cardiovalvulotome, *J. Exper. Med.* 40: 375 (Sept.) 1924.

many prominent surgeons spoke discouragingly concerning the subject. Del Vecchio<sup>7</sup> experimentally incised the hearts of dogs, then sutured the wounds, and the animals recovered. In 1895, he demonstrated these healed wounds to the Eleventh International Medical Congress in Rome, Italy. During the following year, three human hearts were sutured; the first two patients died following the operation, while the third (operated by Rehm<sup>8</sup>) lived and returned to normal life.

In 1920, Tuffier<sup>9</sup> collected 305 cases of sutured wounds of the heart, in 50.4 per cent of which the patients recovered. This probably is a rather high percentage because surgeons are more prone to report their successful cases.

The prognosis depends on the type and extent of the injury. Wounds which penetrate into the cardiac cavity and leave an opening in the heart wall sufficiently large for the escape of much blood are usually fatal in a short time. The clinical picture of the less extensive wounds depend largely on the size of the opening in the pericardium. If there is a fairly large opening providing free escape of blood, the symptoms produced are those of any severe hemorrhage. If the pericardial rent is small and blood collects in the pericardial cavity, compression of the heart results; the arterial pressure is lowered, and the venous pressure is elevated. When the intrapericardial pressure becomes equal to the venous pressure, the heart ceases to function; this condition is called heart tamponade. During the process of compression (or tamponade) cyanosis develops, the pulse grows weaker and more rapid, heart sounds become distant, and respiration is increased.

A surgeon may be called to meet a cardiac emergency at any time; therefore, he should be familiar with the various methods of operative technic, and know how they can best be applied under different conditions. The earlier operations were performed through an opening obtained by the removal of one rib. This, however, gave poor exposure. Later methods include: (1) removal of two or more ribs and costal cartilages subperiosteally; (2) hinged flaps consisting of skin, muscles, ribs and possibly a portion of the sternum; (3) median sternotomy; (4) intercostochondral thoracotomy—that is, two, three, or four costal cartilages are divided near the sternum and the ribs retracted until sufficient exposure is obtained. The last two methods are probably the most satisfactory. Median sternotomy gives the best exposure of the

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7. Del Vecchio, S.: *Sutura del Cuore*, *Riforma med.* 11:38, 1895; quoted from Beck.

8. Rehm, L.: *Ueber penetrierende Herzwunden und Herznaht*, *Arch. f. klin. Chir.* 55:315, 1897; quoted from Beck.

9. Tuffier, T.: *La chirurgie du coeur*, Cinquieme congres de la Societe Internationale de Chirurgie, Paris, July 19-23, 1920; *Extrait*, Brussels, Haye, 1920; quoted from Beck.



anesthetic being used. The edges of the wound were retracted, and the pulsating heart was seen in a pool of blood.

A suture was placed in the apex of the heart; this was used for traction by holding it in the left hand, while the left index finger examined the heart carefully. There was a longitudinal incision 3 cm. long in the anterior portion of the right ventricular wall, extending to a depth of about 6 mm. Owing to the length of the wound, hemostatic sutures were not used. The index finger held over the wound controlled the bleeding, while interrupted silk sutures were applied to approximate and close the edges of the wound. When this was accomplished bleeding ceased. All the blood was then cleared out of the pericardial cavity; this afforded an excellent view of the wound, which was about 5 mm. from the coronary artery. None of the sutures had pierced or included that structure. The pericardium was closed with interrupted silk sutures, which did not make an air-tight pericardial cavity. There were three openings (each about 15 mm. in diameter) in the left pleural cavity; these were not closed. The wall of the chest was closed air tight. A needle was inserted into the left pleural cavity and about 1,500 cc. of air removed, thus relieving the pneumothorax.

During the first thirty-six hours after the operation the temperature was between 99 and 100 F., the pulse rate between 100 and 126, and the respiration from 58 to 70. The patient's breathing was shallow, and there was some air hunger. He was thirsty, took fluids well, and retained them. His temperature then rose and for four days remained between 101 and 102.4 F. The heart rate averaged around 130 and went up as high as 152. The respiration gradually went down to around 40. Nourishing foods were given, he was digitalized and treatment with small doses of digitalis continued.

July 19: Examination showed pneumonia of the base of the left lung. Pericardial effusion and dulness (extending 6 mm. to the right of the midline) were present, and a pericardial friction rub was heard.

July 22: The left border of the area of cardiac dulness extended to the anterior axillary line and the right border 10 cm. to the right of the midline. There was evidence of fluid in the left pleural cavity at that time. Slight separation of the edges of the wound, with the drainage of a small amount of pus, was noted.

July 24: The pericardial cavity was aspirated through the fourth interspace just to the right of the sternum, and 110 cc. of straw-colored fluid was obtained. The left pleural cavity was aspirated, and only 50 cc. of bloody fluid was obtained. *Staphylococcus aureus* was cultured from the pericardial fluid and from the pus of the wound. The pleural fluid was sterile.

July 26: Two hundred cubic centimeters of fluid was aspirated from the pericardial cavity (fig. 1). *Staphylococcus* was again grown from the fluid. The wound was entirely open, exposing the anterior mediastinum. The pleural cavity was walled off and did not communicate with the wound. A roentgenogram showed bronchopneumonia of the base of the right lung in addition to the large bottle-shaped cardiac shadow and the radiopacity of the base of the left lung.

July 30: The cough increased and was aggravating. Only 50 cc. of fluid was obtained from the pericardial cavity; the fluid was lost, so culture was not obtained.

August 4: One hundred and fifty cubic centimeters of sterile fluid was aspirated from the pericardial cavity. The patient seemed stronger, but the temperature remained around 101 F.; the pulse rate was 140, and the respiration, 50.

thorax. The right side of the diaphragm was less active than the left. The heart was slightly globular (water bottle type), the enlargement being especially to the right. Fluid was not seen in the pericardium. The bullet was immediately to the left of the midline, moving with each heart beat and lying close to the anterior wall of the chest. Fluoroscopic examination two hours later did not show any change in the condition.

Operation was performed about three hours after admission by Dr. Victor Hill. A midline incision was made down to and through the sternum from the ensiform cartilage to the attachment of the fourth costal cartilage, where the incision was carried laterally through the left side of the sternum into the fourth interspace. When the left portion of the sternum was retracted, the pericardium was exposed. This was incised and retracted, and there was little fluid in the pericardial cavity. A darkened area could be seen on the anterior portion of the right ventricular wall where the bullet could be felt deep in the heart. A suture was placed in the apex of the heart for traction, according to the technic described by Beck.<sup>23</sup> A suture was then placed in the heart muscle on either side of the bullet. The bullet was removed with a hemostat and a large stream of blood spurted from the wound. The two sutures that had been placed on either side of the wound were then pulled to the opposite side from which they were placed, which thoroughly controlled the bleeding. The wound was then closed with interrupted figure-of-eight silk sutures. (Six of these sutures were used.) The pericardium was closed with interrupted sutures of silk. The sternal reflection was put into place and sutured with kangaroo tendon.

The temperature rose to 103 F. the following day, the pulse steadily increased in rate and became weaker. There were moist râles in the right lung; the left lung seemed clear, but sounds were distant. The patient reacted poorly, and died forty-eight hours following operation.

Postmortem examination showed only a small amount of fluid in the pericardium. The sutures in the heart muscle were removed. The wound extended a distance of 15 mm. into the interventricular septum with a lateral perforation into the cavity of the right ventricle. The left lung was collapsed and airless. There was a slight diminution of crepitation in the right lung.

CASE 2.—H. M. A., a colored man, aged 26, was admitted to the Louisville City Hospital on July 16, 1927, with a stab wound 8 cm. in length and extending from the tip of the ensiform cartilage slightly upward and to the left. The patient presented the general picture of shock: The pulse was 160 and weak; the skin was cold and moist; every time he breathed a slushing sound was produced, and considerable blood was sprayed from the wound. He was under the influence of alcohol, which may have contributed toward his semiconscious condition.

An attempt was made to combat shock by subcutaneous infusion of saline and caffeine sodium benzoate, application of external heat and hot coffee by rectum.

After the patient was in the operating room, which was about two and a half hours following the accident, examination showed that the tip of the ensiform cartilage and the cartilages of the fifth, sixth and seventh ribs were cut. Although this opening, which was already made, gave a rather low exposure of the heart, it was fairly satisfactory. The skin and subcutaneous tissues surrounding the injured area were infiltrated with 1 per cent procaine hydrochloride, no other

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13. Beck, Claude S.: Wounds of the Heart, *Arch. Surg.* 13:205 (Aug.) 1926.

digitalis, limitation of the fluid intake and methods favoring the excretion of fluids. Merbaphen was given repeatedly at from two to five day intervals; a large output of urine followed the use of this drug, and there was a noticeable reduction of edema.

Edema was not noticeable after October 7. The wound had healed. The fluid intake was gradually increased, and was well tolerated. Antisyphilitic treatment was started.

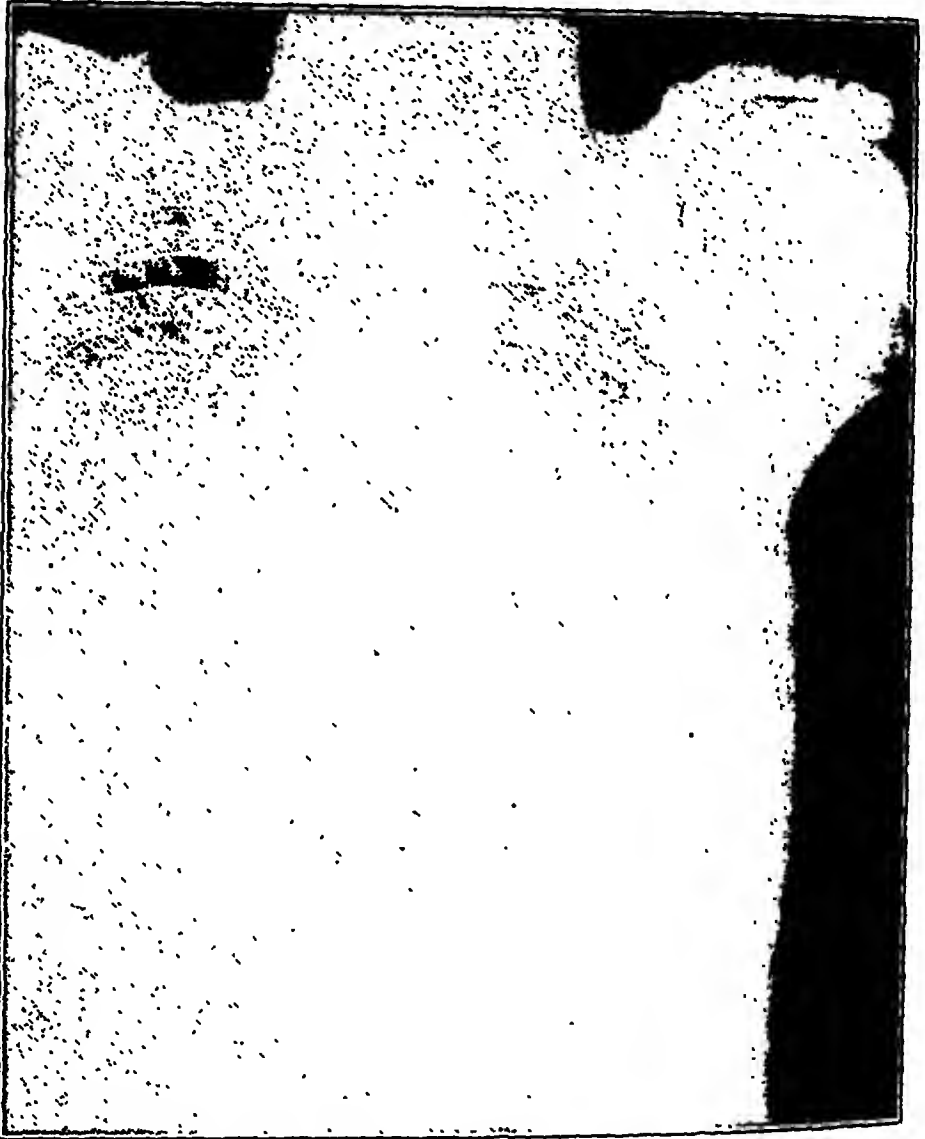


Fig. 2.—Roentgenogram taken Aug. 22, 1927, showing fluid in both pleural cavities.

October 20: The patient was allowed out of bed. He would not take exercise gradually, but walked about at will the second day he was up; he did not suffer any ill effects, and continued to go about as a normal person.

October 30: He was discharged from the hospital in apparently good physical condition; the fields of both lungs were clear, and his heart was 12 cm. in its greatest diameter (fig. 3).

November 9: He was seen for the last time, and seemed normal.

August 13: One hundred and fifty cubic centimeters of sterile fluid was aspirated from the pericardial cavity. The temperature was 100 F.; the pulse rate, 120, and respiration, 40. The patient's condition was much better, although he continued to have an irritating cough. The chest wound was clean and granulating.

August 20: The patient was so well that he was allowed to sit up for a short while. The temperature had been normal for six days previously.

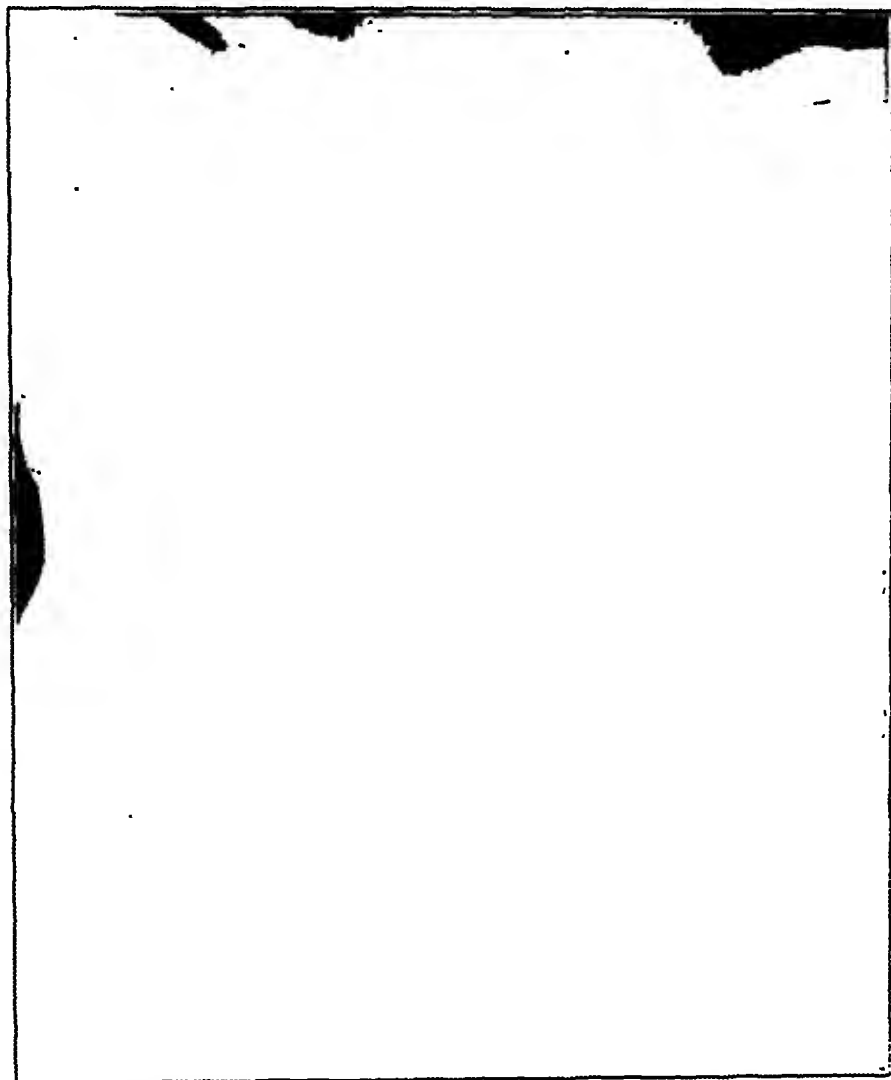


Fig. 1.—Roentgenogram taken July 26, 1927, showing enlargement of the cardiac shadow, bronchopneumonia at the base of the right lung and radiopacity of the base of the left lung.

August 22: Dyspnea and generalized anasarca was found on examination (fig. 2).

During the next six weeks, general treatment was given for cardiac decompensation, the etiology of which was considered to be myocardial injury, adhesive pericarditis or both. The treatment in general consisted of the administration of

irritant to the pericardium cause either pericardial effusion or adhesions or both. Small amounts of blood would be injected into the pericardial cavity, the blood would be absorbed, and effusion or adhesions did not develop. These experiments bring out forcibly that it is most important to produce as little trauma as possible. The sponging of the blood from the cavity with gauze produces trauma and suction should be substituted when possible.

The associated pneumothorax may be a factor in lowering the resistance of the patient. Therefore, when feasible, it would seem advantageous to close the thorax tight and remove the air from the pleural cavity.

Aspiration of the pericardial cavity is a procedure not entirely free from danger. A coronary artery may be punctured, the pericardial cavity becoming filled with blood, and fatal tamponade result. Owing to this possibility—such an accident has occurred—suppurative pericarditis should be treated by open incision when the condition of the patient warrants that procedure. Ordinarily, the best location for the insertion of the needle, when aspiration is to be performed, is just below to the left of the ensiform. This is the only location where the pericardial cavity may be entered without penetration of the pleural cavity. This location was not selected in my case, because the obviously infected wound was at that site.

NOTE.—The patient returned to the hospital on May 1, 1928, in perfect health. He said that he had not had any cardiac embarrassment since leaving the hospital.

## COMMENT

The method of handling the heart by the traction suture in the apex enables the procedure to be carried out with much less trauma than by any other method now known. The placing of sutures alongside the wound to control hemorrhage prevents soiling of the operative field.

Many of the early operators left a drain in the pericardial cavity. Adhesive pericarditis almost invariably followed these cases. In most of

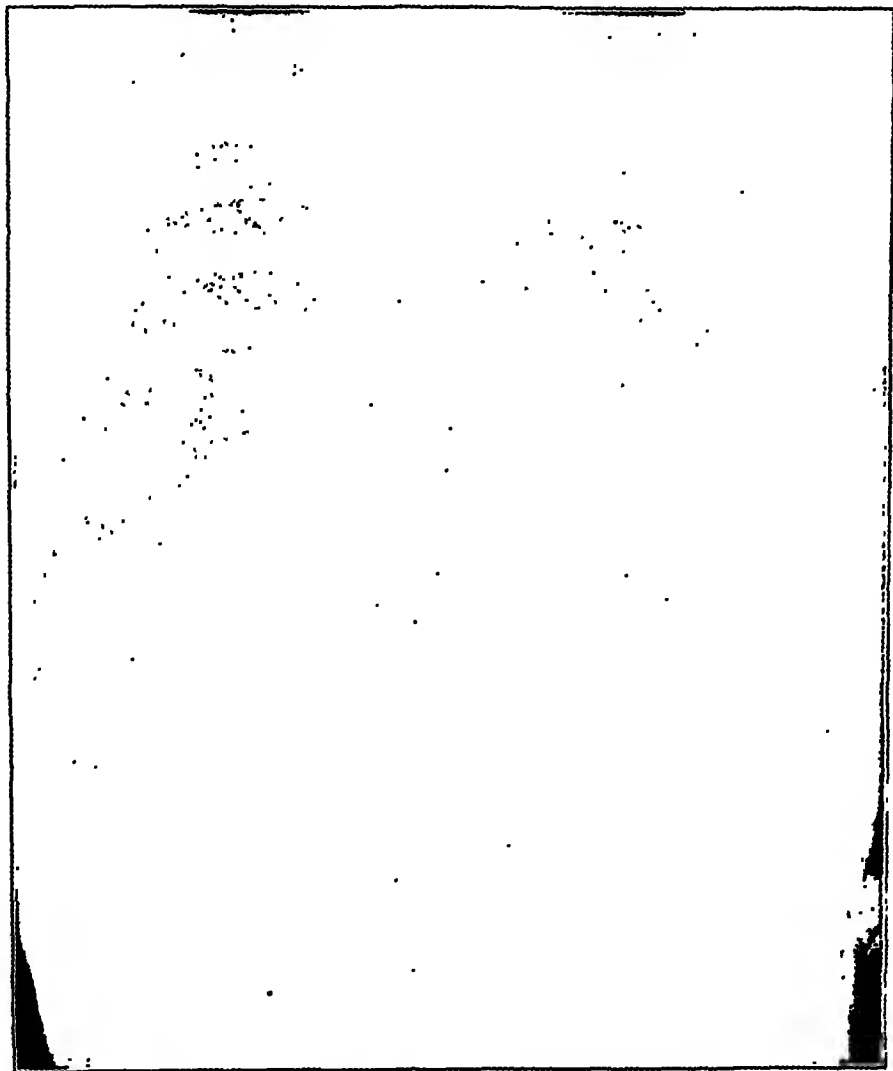


Fig. 3.—Roentgenogram of patient just before leaving hospital on Oct. 30, 1927, showing a return to almost normal.

those cases in which drainage was not used, pericardial effusion developed. These observations led to some experimental work by Beck and Moore,<sup>14</sup> who found that mild trauma and the application of a chemical

14. Beck, C. S., and Moore, R. L.: The Significance of the Pericardium in Relation to Surgery of the Heart, *Arch. Surg.* 11:550 (Oct.) 1925.

that the tendon of the long head was not congenitally absent, but that it had secured a secondary attachment after division. Since neither my associates nor I have seen a single convincing case of congenital absence of the tendon of the long head in adults, in more than a thousand arms, it is clear that this condition is rare, although absence of the long head is common. Indeed, the high incidence of the latter itself compels another interpretation than that of developmental anomaly alone.

In previous publications,<sup>6</sup> I have tried to convey the idea that partial or complete destruction of the articular portion of this tendon is relatively common and not unique, as King and Holmes<sup>7</sup> seem to imply.



Fig. 1.—Left scapula, illustrating the apparently total fusion of the long head of the biceps with the dorsal portion of the ligamentous lip.

I have thirty-nine examples of dislocation and twenty of complete absence of the articular portion of this tendon in my possession at present. Although only six of the cases of dislocation are maximal, cases in which the tendon had passed completely over the lesser tuberosity,

6. Meyer, A. W.: Unrecognized Occupational Destruction of the Tendon of the Long Head of the Biceps Brachii, *Arch. Surg.* 2:130 (Jan.) 1921; Further Observations Upon Use-Destruction in Joints, *J. Bone & Joint Surg.* 4:491, 1922; Spontaneous Dislocation of the Tendon of the Long Head of the Biceps Brachii, *Arch. Surg.* 13:109 (July) 1926; footnote 1.

7. King, Jennings M., and Holmes, George W.: The Diagnosis and Treatment of Painful Shoulders, *J. A. M. A.* 89:1956 (Dec. 3) 1927.

# SPONTANEOUS DISLOCATION AND DESTRUCTION OF TENDON OF LONG HEAD OF BICEPS BRACHII

FIFTY-NINE INSTANCES \*

A. W. MEYER

PALO ALTO, CALIF.

In bringing these two conditions together in the title, I am not assuming that they necessarily are always associated and that every case of destruction of this tendon necessarily was first one of dislocation. In most cases, however, dislocation of the tendon probably leads to greater wear, but, as reported previously,<sup>1</sup> tendons still lying in a normal position and in otherwise normal shoulder joints may show considerable wear.

Since the biceps as well as other muscles may be congenitally absent, it follows that the tendon of either head may also be absent congenitally, but it is improbable that all the statements in the literature on this matter can be taken at their face value. I never have seen a clear case of congenital absence of the long head since I have understood the condition better, and few of those reported in the literature, including my own,<sup>2</sup> are absolutely convincing in view of the facts I have subsequently revealed. Such cases as those spoken of by Lauth<sup>3</sup> and Lecco<sup>4</sup> seem unequivocal, but what is needed is examination of the tendon in a large series of the new-born.

I do not believe that the prominence of the supraglenoid tubercle is a reliable criterion for deciding whether the tendon of the long head is congenitally absent; for, as shown in figure 1, the tendon of the long head frequently merges so completely with the ligamentous, glenoidal lip as to be indistinguishable and also inseparable from it. One could therefore expect great variations in the prominence of the tubercle for this reason alone. In such cases as that reported by Craig,<sup>5</sup> the downward extension of the so-called transverse humeral ligament suggests

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\* From the Department of Anatomy, Stanford University.

\* This does not include a number of instances in the twenty-five bodies under dissection this year.

1. Meyer, A. W.: Further Evidences of Attrition in the Human Body, *Am. J. Anat.* **34**:241, 1924.

2. Meyer, A. W.: Absence of the Tendon of the Long Head of the Biceps, *J. Anat. and Phys.* **48**:...., 1913-1914.

3. Lauth, Ernest Alexandre: *Nouveau manuel de l'anatomiste*, Paris, 1829.

4. Lecco, T. M.: Ein Fall von vollständigen Fehlen des langen Kopfes des M. biceps brachii und die damit in Zusammenhang stehenden Veränderungen an Knochen und Gelenktheilen, *Anat. Anz.* 1907, vol. 30.

5. Craig, Joseph D.: Anomaly of the Long Tendon of the Biceps Muscle of the Arm, *New York M. Record*, 1899, vol. 56.



published a photograph (fig. 7) of a relatively early case without interpreting it as such. The paired humeri represented in figure 2 illustrate a still earlier stage in a case of dislocation. The condition of the sulcus on the left humerus represents an earlier stage than that on the right, for in the latter the tendon had already left the proximal part of the sulcus and had come to play on its anterior wall and crest and on the lesser tuberosity. In all the cases of dislocation I have seen, the tendon still occupied the sulcus in the region distal to the tuberosities. As the sulcus is shallow here, it is difficult to see how it would be possible to determine the absence of the tendon by palpation, and those



Fig. 2.—Paired humeri, illustrating instances of beginning dislocation. The widening of the proximal portions of the sulci should be noted.

who have claimed that they have found the sulcus empty in the living, must of necessity have determined this by palpation through skin, subcutaneous tissues, fasciae and the thick layer of muscles (pectoralis major and deltoid) overlying the more proximal portion of the sulcus, which is the only region in which dislocation is known to occur spontaneously; that is, gradually from use.

Since the bodies used in the anatomic laboratory at Stanford University are not drawn from an unusual source but represent the classes and occupations usually represented in this material, I see no reason why the incidence of bicipital dislocation in this laboratory should be

most all of the rest are wholly unequivocal to any one familiar with the condition. In all the cases of absence of the articular portion, the tendon had obtained a secondary attachment to the floor or sides of the sulcus or to the humeral diaphysis directly distal to the lesser tuberosity, as represented in figures 4, 5 and 6.<sup>8</sup>

Although complete absence of the intra-articular portion (destruction) occurred more frequently on the right than on the left, the opposite is true of dislocation; however, since both series still are small, not much importance can be attached to conclusions drawn from them. Thirteen cases of complete destruction occurred on the right and seven on the left, and seventeen cases of dislocation occurred on the right and twenty-two on the left. Both sexes are represented, and in four cases the dislocation was bilateral. As I did not preserve all cases of destruction of the tendon because they are so common, and did not discover such a possibility as spontaneous dislocation until a few years ago, it is probable that I will be able to extend these observations considerably during the next few years. Many cases probably were overlooked.

I realize that the word spontaneous is out of place here as elsewhere, but I am using it to distinguish these cases of dislocation from those resulting from sudden trauma due to exertion or to external causes. Some trauma undoubtedly is associated with these cases of gradual occupational dislocation, but trauma, in the ordinary sense, is not a factor. Nor do I wish to rule out chronic arthritis. Evidences of its presence are unmistakable in some cases, but there is no reason to suppose that people afflicted with chronic arthritis thereby become immune to dislocation. They would, of course, be more likely to suffer it because of the changes in bone and capsule associated with this disease.

In some cases in which the divided tendon obtained a secondary attachment to the diaphysis distal to the lesser tuberosity, it may have been dislocated and have played on the tuberosity before it was divided; hence it is possible that most of these cases should really be included among cases of dislocation. It is not improbable that this also is true of the cases in which the tendon is attached to the floor of the sulcus in the region of the lesser tuberosity, for it is not necessary for the tendon to be exposed to considerable wear from contact with the relatively rough face of the lesser tuberosity, in order to be weakened by wear.

#### PARTIAL DISLOCATION

Since the observations published in 1926, I have found that partial dislocation of this tendon is a far commoner condition in bodies in our dissecting room than I had surmised. As stated at that time, I did not recognize the cases of beginning dislocation at first, and in 1924, I

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8. Meyer (footnote 6, first reference).

The relation of the tendon to the head of the humerus, and to the floor of the intertubercular sulcus, necessarily changes as the position of the arm changes, for both shift beneath it. When the arm is in slight lateral rotation, the under surface of the tendon lies fully on the floor of the sulcus; but as lateral rotation is increased, its anterior margin is forced against the anterior wall of the sulcus, especially that portion formed by the lesser tuberosity and the capsular attachment proximal to it. In medial rotation, on the other hand, the anterior wall of the sulcus and the adjacent capsular attachment become the surfaces which the tendon uses as a trochlea, while its dorsal margin is forced against the dorsal wall of the sulcus.

It is evident that the tension exerted on the capsular attachment proximal and superior to the lesser tuberosity varies with the position of the arm and the disproportion in width between the tendon and the sulcus, as well as with the force exerted by the muscle on the tendon. It seems probable that the greatest tension is exerted on this portion of the capsule which is the first and chief obstacle to forward dislocation especially in the position of extreme lateral rotation during partial abduction. This is the position frequently reached in occupations that require shoveling. In extreme abduction the relations would be entirely different, and the tendency to dislocation would probably be slight because of the approximation of the lesser tuberosity to the supraglenoid tubercle.

The tendency to dislocation of this tendon, which exists in all normal shoulder joints, is opposed primarily by the attachment of the articular capsule in the region proximal to the lesser tuberosity. Contrary to the usual statement, I do not believe that the so-called transverse humeral ligament is an important factor for preventing dislocations, for I have seen cases in which the tendon was entirely normal in position, although this ligament was extremely weak or absent. Moreover, after observing the condition of the intertubercular portion of the capsule, I fully concur in the omission of a name for this so-called ligament from the Basle nomenclature. Transverse fibers bridging the sulcus, which could be designated properly as a ligament, seldom are present, and when this is the case, they usually are located farther distally than the intertubercular region, in which the transverse humeral ligament of Brodie is supposed to occur.

I have seen only one case of complete ossification of the intertubercular portion of the capsule and another in which ossification was partial. In the former, the tendon passed through a bony canal about 2 cc. long as in the mole, armadillo and musk ox, and in the latter case it was covered medially by an exostoses. It is such rare instances as these that may have phylogenetic significance and hence justify the term transverse humeral ligament, but careful developmental and statistical studies are necessary to establish this.

unusual. With a few exceptions, practically all the bodies are of persons who belonged to the working classes. The great majority were Caucasian, only a few having been negroes, Chinese, Mexican and Hindus.

The greater frequency of absence of the intra-articular portion of the tendon on the right side may be due to right-handedness, and the somewhat larger frequency of dislocation on the left may be due to the fact that greater tension is put on the tendon and the capsular attachment on this side, in occupations that require shoveling and pitching with a fork, for the left hand acts as fulcrum and the left humerus passes into marked lateral rotation and abduction in every such movement.

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#### ANATOMIC FEATURES

In considering the anatomy of the humeroscapular articulation, one is impressed with the fact that the normal conditions promote dislocation of the tendon of the long head. Until the arm is abducted somewhat, the tendon curves forward, encircling the slippery and sloping, rounded surface of the upper, anterior portion of the head of the humerus. As tension on the tendon is increased, it tends to displace the latter backward and downward. This does not imply, however, that a gap, such as appears in roentgenograms of the shoulder with the arm at rest, exists between the head of the humerus and the acromion. Muscle tone alone always must keep these in contact. The large gap seen in roentgenograms of the shoulder is due, of course, to the presence of the articular cartilage and capsule and the tendon of the supraspinatus, and is magnified because the lower surface of the acromion and the cartilage on and the underlying compacta of the humeral head, are curved bodies. Since the humero-acromial interval is decreased decidedly in all cases of destruction of the upper portion of the capsule and the tendon of the supraspinatus and also by wear on the under surface of the acromion and on the articular cartilage of the humeral head, this decrease should be evident in roentgenograms.

Although the articular cartilage on the humerus is sometimes grooved slightly by the tendon in the region adjacent to the tuberosities, this sulcus is too shallow to have much, if any, influence in maintaining the normal position of the tendon, and only that portion which lies between the tuberosities in adduction, is properly accommodated by the normal sulcus. The tendon usually widens and flattens decidedly as the supraglenoid tubercle is approached, where it sometimes is three, or more, times as wide as in the intertuberosital portion, when the arm is at rest. Since anatomists now speak of the entire bicipital sulcus as intertubercular, I am using the word intertuberosital to designate the portion between the greater and lesser tuberosities.

present, (5) the capsular attachment may be weakened by intracapsular bursae and (6) the capsular attachment to the anatomic neck in the region proximal to the lesser tuberosity may be restricted.

#### INTRAMURAL BURSAE

So far as I know, the presence of bursae in the capsular attachment in this region has not heretofore been reported; yet, not infrequently, one or two small intracapsular supraperiosteal bursae are present. The presence of these bursae in this region of capsular attachment results in the weakening of it. I am not certain as to the genesis of these bursae, but I do not believe that they are congenital, but rather that they result from the play of the tendon of the long head against and on this portion of the capsular attachment, especially during marked lateral rotation. Not infrequently the bursa of the subscapularis also extends far up under the tendon of this muscle, and it may even communicate with the sheath of the long head in the intertubercular sulcus. This may also be the case with the intracapsular bursa or bursae which form a gap bridged by the capsule or the tendon of the subscapularis, as the case may be. Such defects in the capsular attachment must greatly facilitate dislocation of the tendon, for they weaken the primary obstacle against its inception. Although the articular capsule and the tendon of the subscapularis always fuse intimately, it is only the capsular attachment which is an obstacle to dislocation, for the dislocated tendon of the long head does not detach the tendon of the subscapularis but comes to lie on it in far advanced cases, as illustrated in the figures referred to. If the capsular attachment to the bone in this region is maintained and stretches, the tendon of the long head comes to lie in a capsular sling, as shown in figure 4. This necessarily protects it against attrition on the face of the lesser tuberosity. Under these circumstances, it may become dislocated without showing much or even any wear from contact with the lesser tuberosity, and such cases are not rare.

Since in all the cases of detachment of the tendon of the subscapularis over practically the entire lesser tuberosity some arthritic reactions are shown, it seems to me that the gradual dislocation of this tendon probably results from disease, although mechanical factors are involved. In some cases the tendon of the subscapularis retains an attachment anterior and distal (below) to the lesser tuberosity only, and looks as though it had undergone a slow migration from the region of its wide normal attachment. It must not be overlooked, however, that abnormalities in the attachment of this tendon may also be concerned in this matter.

Spontaneous dislocation of the tendon of the long head of the biceps may occur without the presence of arthritis, a supratubercular

The nature of the anterior wall of the sulcus necessarily is an important factor in dislocation. This applies especially to the presence or absence of the bony ridge shown in figure 3, which I have called the supratubercular ridge. Although this name might imply that it is related to either tuberosity, I have never seen it related to the greater. It extends obliquely forward and downward from the region of the articular cartilage to the upper and dorsal portion of the lesser tuberosity. As the surface of the distal extremity of this ridge is on a level with the surface of the latter, and since the tendon plays on it



Fig. 3.—Portion of a right humerus with a supratubercular ridge marked X.

much as the tendon of the peroneus longus plays on the trochlea of the cuboid, its rôle in dislocation is plainly evident. In a study made by Cilley (unpublished) it was present in 17.5 per cent of 200 humeri.

In all normal joints there are three, and there may be six, factors which favor dislocation of this tendon: (1) the normal course of the intracapsular portion of the tendon and its relation to the humeral head, (2) the much greater width of the proximal portion of the tendon, (3) the fact that the anterior wall of the sulcus which is formed by the lesser tuberosity normally acts as a trochlea for the tendon in the usual position of medial rotation, (4) a supratubercular ridge may be

Not infrequently the floor of the intertubercular sulcus slopes decidedly toward the greater tuberosity in its upper extent, thus tending to throw the tendon against the dorsal wall of the sulcus and facilitating wear on this margin, as shown in figure 5. The first instances of this kind which I saw led me to think that the wear of the tendon here must have resulted mainly from its being caught between the greater tuberosity and the acromion, after a defect had been formed in the articular capsule; but the subsequent finding of worn tendons in joints with intact, normal capsules made this interpretation untenable. I have also found that the tendon can be dislocated without previous detachment of the articular capsule, for the latter may merely stretch in the region of the lesser tuberosity instead of becoming detached.

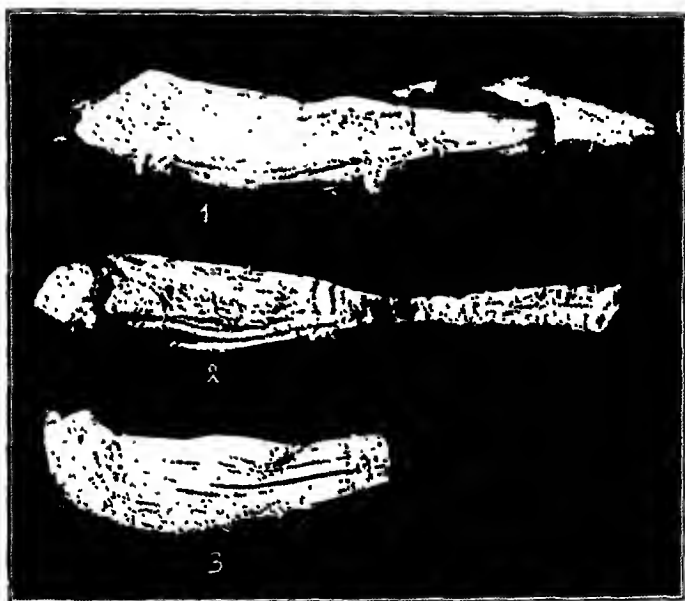


Fig. 5.—Three left bicipital tendons from otherwise wholly normal joints, showing wear along the dorsal margins. The reflection of the tendon sheath is clearly shown in number 1. All the tendons were cut close to their origin.

The fraying of its dorsal margin manifestly is produced by contact with the dorsal wall of the sulcus and is especially marked in tendons which are much wider in their proximal portions. Fraying of this edge may extend to within 0.5 cc. of the supraglenoidal attachment. I do not know whether or not wear on this margin, under otherwise normal conditions, would ever be sufficient to divide the tendon, but I am inclined to doubt it. It could, however, not fail to weaken it and thus facilitate its rupture.

In some cases in which the tendon had ruptured some distance from its place of origin, the proximal fragment could be recognized, although it had become adherent to the inner surface of the capsule. Often it

ridge or bursae in the region of the capsular attachment, and also without the restriction of this attachment to the upper margin of the lesser tuberosity. Although it must remain a matter of opinion as to just what constitutes beginning dislocation, I think it conservative to say that approximately 4 per cent of the bodies and 8 per cent of the



Fig. 4.—A right humeroscapular articulation with the tendon reflected anteriorly to reveal its bed. The proximal portion of the intertubercular sulcus is seen to the left of the new bed of the tendon. This tendon, which has been in a sling, had passed practically over the lesser tuberosity but still occupied the sulcus distal to the intertuberosital region.

tendons illustrate some stage of this process. A sufficient number of these cases present no evidences of pathologic conditions to refer to arthritis as a primary or sole cause.



In view of the undoubted commonness of destruction and dislocation of the tendon of the long head of the biceps, it is especially regrettable that clinical histories are not available. This is no one's fault, of course, for it is unlikely that any of the persons so affected sought relief from conditions of long standing by seeking medical care during later years. Moreover, the medical staffs of relief homes, almshouses and insane asylums are too small to permit much attention being given to slight disabilities or aches felt by the aged. However, although they remained unknown until recently, the conditions nevertheless are of peculiar scientific interest and also of great practical importance, for they undoubtedly were sustained during the most active years of the person's life.

#### SUPERNUMERARY CAPSULAR HEADS OF THE BICEPS

While studying the humeroscapular articulation in specimens at hand, I found three cases in which the biceps had a third tendinous or capsular head. In two specimens with unruptured tendons, these tendinous cords arose from the tendon of the long head in the region of the lesser tuberosity and extended to the upper anterior and inner surface of the articular capsule. These cords fused completely with the inner surface of the capsule and gradually thinned out as they continued toward the region of the supraglenoid tubercle. They are, however, entirely distinct from the long head and have exactly the same structure, although the largest is only half as thick as the entire tendon. The presence of such a capsular head would tend to prevent too great a retraction of the long head when the latter is divided, and thus would facilitate its secondary attachment in the region of the lesser tuberosity. It also seems that the traction exerted on the capsule by it might cause discomfort if not pain, especially in cases in which the tendon of the long head had stretched because of weakening from attrition.

These capsular heads of the biceps mentioned by Moser, Henle and Welcker, left the posterior and upper surface of the main tendon in the region of reflection of the synovial sheath. The largest lay adjacent to the main tendon, but one of the smaller occupied a separate, superimposed compartment. The former could be traced along the under surface of the capsule as far as the ligamentous lip of the glenoid cavity, in the region of the supraglenoid tubercle, but they were an unmistakable portion of the tendon of the long head. In the third case the supernumerary tendon lay outside of the synovial sheath of the tendon of the long head, but joined the capsule in the same region as the others. It widened out considerably distally and apparently joined the tendon of the pectoralis major. Too much had been removed in dissection to enable me to follow it further distally, but since it was attached throughout its extent along

could not be traced without difficulty, and in some cases not at all. Its fusion with the capsule may be due to traumatism, and its atrophy to disuse.

Although the incidence of spontaneous dislocation—and destruction—in the general population undoubtedly is far less than in the material in the dissecting room, it must be exceedingly common in persons who work in lumber and construction camps and in mines. Although the condition here described is undoubtedly chronic, it must be more or less distressing, even if not disabling, until maximal conditions are reached. In cases in which the intertubercular sulcus has not undergone secondary changes which have resulted in narrowing or roughening of it, relocation of the tendon, if not too badly worn, would seem justifiable if the tendon can be secured against recurring dislocation. Little could

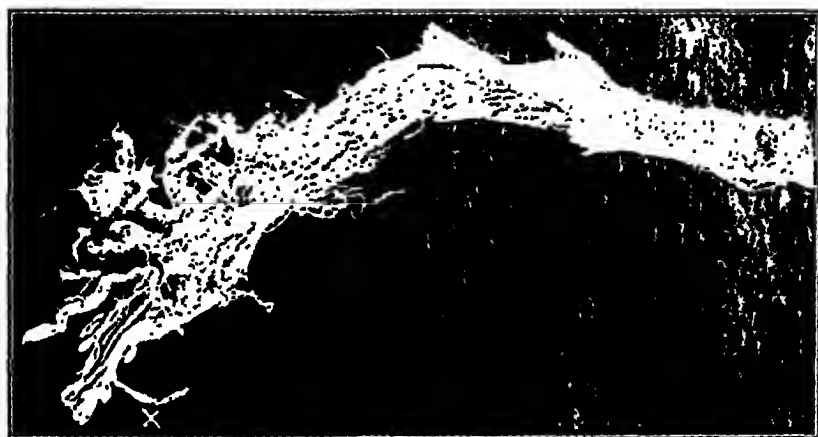


Fig. 6.—Right tendon of the long head photographed from beneath, showing maximal wear. This tendon was attached only by a fine strand marked x, in the normal region and shows wear all the way down to the region of the reflection of its synovial sheath.

be accomplished, however, by relocating such a tendon as shown in figure 6, though it could be fastened securely to the diaphysis so as to restore normal tension on it and thus prevent a certain amount of atrophy of the lateral portion of the muscular belly of the biceps.

Except in early stages, I doubt, however, whether much can be gained in muscular power by reattachment of the tendon of the supraspinatus, so commonly divided by attrition, or displaced dorsally in cases of attrition. To reintroduce what remains between the bony surfaces involved might merely reestablish former disabilities, for the shortened tendon and muscle would have to be stretched considerably and would again be subjected to disastrous wear unless the patient changed his occupation.

tuberosity, or to the floor of the sulcus in this region, or still more infrequently to both walls of the sulcus, a portion of the frayed tendon being drawn to each side by the tendon sheath in the region of reflection of the latter.

5. In some cases in which the tendon is divided near the supraglenoid attachment, it retracts completely before it obtains a secondary attachment, with great lengthening of the extracapsular portion—even up to 100 per cent—and marked atrophy of the lateral belly of the muscle and resultant asymmetry.

its dorsal border in the region of the intertubercular sulcus and was fused so completely with the fascia proximal to the tendon of the pectoralis major, it is unlikely that it had a muscular component distinct from the biceps, and even if it did these supernumerary tendinous heads are totally different than the well known third muscular head of the biceps so commonly present.

None of these capsular heads could have developed from a portion of the synovial sheath which became strengthened through tension made on it, and since the tendon of the long head develops wholly outside of the articular capsule, and completes its migration inward as late as the third month of prenatal life, it need not surprise one that a portion of it may become stranded and fuse with the articular capsule through which it must pass. Indeed, it seems as though the entire tendon should some time be found in an extracapsular position. As far as I know this has not been observed. The tendinous component which arose from the articular capsule and ended near the tendon of the pectoralis major, if not in it, seems comparable to the glenobrachial muscle of Gruber; but since the other capsular heads here reported are supernumerary, they differ from cases in which all of the tendon of the long head arises from the joint capsule. It seems probable to me that anomalies such as these well may give rise to symptoms and thus make diagnosis of obscure conditions of the shoulder still more difficult. Any one especially interested in these heads will find them considered by Welcker.<sup>9</sup>

#### CONCLUSIONS

1. Uncomplicated, partial or complete, spontaneous forward dislocation of the supratuberosital and intertuberosital portions of the tendon of the long head of the biceps, on to or over the lesser tuberosity as far as the tendon of the subscapularis, is common in laborers past middle life.

2. This dislocation may be due to gradual stretching, detachment or destruction of the capsule proximal to and in the region of the lesser tuberosity.

3. Wear of the tendon along its dorsal margin may occur in otherwise normal joints, but wear throughout its width probably is frequently due to contact with the lesser tuberosity in cases of dislocation, or with the greater tuberosity and acromion in the course of destruction of the dorsal portion of the articular capsule, unaccompanied by dislocation.

4. After division by attrition, the tendon usually obtains a secondary attachment to the humeral diaphysis immediately distal to the lesser

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9. Welcker, Hermann: II. Ueber Muskelvarietäten, *Ztschr. f. Anat. u. Entwgsch.*, 1876, vol. 1.

Sherrington found that in the jejunum 40 cm. below the pylorus, the intrajejunal pressure varied between 2 and 4 cm. of water.

By a slightly different procedure, we have confirmed these observations of the normal intra-intestinal pressure in dogs, and at the same time we have noted something of the relationship of the intra-abdominal pressure to that within the intestine in which obstruction has been produced. We share the view of Emerson<sup>3</sup> that a slight positive pressure normally exists within the abdomen, that it is dependent for the most part on the tonus of the abdominal musculature and that normal alterations are due chiefly to the contractions of the diaphragm, change in tonus of the abdominal wall and variations in the bulk of the abdominal viscera.

During the course of this study, we have made observations on the intra-intestinal pressure in some eighteen small dogs (from 8 to 12 pounds [3.6 to 5.4 Kg.]) in each of which simple intestinal obstruction had been artificially produced. The obstructions were made for the most part at two levels, one from about 4 to 6 inches (10.1-15.2 cm.) below the duodenojejunal junction, the other an equal distance above the ileocecal valve. In four animals, the obstruction was made in about the middle of the small intestine. Isolated intestinal loops were made in four other animals, and the pressure recorded within the loop.

#### TECHNIC

Except when otherwise stated, all animals were given  $\frac{1}{4}$  grain (0.016 Gm.) of morphine and ether anesthesia before operation. As strict aseptic precautions were taken as possible. In each case the bowel was doubly clamped and cut across. The lower end was turned in by the Parker-Kerr method and reinforced by a double row of mattress sutures. The clamp was removed from the proximal portion of the bowel and its lumen opened into which the apparatus used was then placed. It consisted of a brass tube about 2 inches (5.08 cm.) in length, with an internal diameter of 3 mm. and a threaded external surface. A concave metal disk about 1.5 cm. in diameter was fixed at one end, and a rubber washer was placed over the disk. A small incision was made in the wall of the bowel about 2 inches proximal to the site of section. The free end of the tube was placed within the lumen of the intestine and brought out through the small incision. The disk fixed one end of the tube within the intestine. The end of the bowel was closed in the same manner as the distal portion. A piece of omentum was then placed over the tube, another rubber washer applied and a second concave metal disk screwed down over the whole, fixing the omentum and the wall of the bowel, not too tightly, between the two rubber washers. A short rubber tube was then attached to the end of the metal tube and brought out through the abdominal wall by a separate stab incision. A small metal clamp closed the rubber tube.

At varying intervals after the operation until the death of the animal, readings were made of the degree of intra-intestinal pressure, and graphic records of the

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3. Emerson, Haven: Intra-Abdominal Pressures. *Arch. Int. Med.* 7:754 (June 15) 1911.

# INTRA-INTESTINAL PRESSURE IN OBSTRUCTION\*

J. C. OWINGS, M.D.

C. A. MINTOSH, M.D.

H. B. STONE, M.D.

AND

J. A. WEINBERG, M.D.

BALTIMORE

The presence of a toxic substance within the lumen of the bowel in cases of intestinal obstruction has long been recognized, but the process by which it enters the system, if indeed it is absorbed, is a problem that is as yet unsolved. The observations of Stone and Fitor,<sup>1</sup> in 1924, suggested the possibility that the changed intra-intestinal pressure might alter the intestinal permeability. Without attempting to investigate the latter problem, it appeared that a study of the degree of pressure within the lumen of the bowel during obstruction might be undertaken with profit.

Before attempting to determine the abnormal conditions, it was necessary to find out the normal intra-intestinal pressure and the relationship of the intra-abdominal pressure to that within the intestine. The physiology of the gastro-intestinal tract from a mechanical point of view reveals an extremely complicated conducting system. The stomach, serving as a reservoir, must receive and readily accommodate the food that arrives often in large volume. Function requires that this mass be stored with little change in the intragastric tension, or else we should experience constant dysphagia, lack of appetite, gastric uneasiness and pain. Sherrington<sup>2</sup> confirmed this and found that the introgastric pressure in an etherized dog over a period of twenty minutes was from  $\frac{1}{2}$  to  $\frac{3}{4}$  cm. of water. The stomach at this time contained portions of a previous meal, but after 450 cc. of water was put into the stomach through a cannula, the pressure rose only to 6 cm. of water and twenty minutes later had fallen to 4 cm. On the other hand, the small intestine has not such great volumes to handle, but receives the products of the antrum pylori in smaller amounts and over a longer period of time. Such being the case, we would expect an intra-intestinal pressure less than that within the stomach. In the experiment already mentioned,

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\* From the Department of Surgery, Hunderian Laboratory, The Johns Hopkins University.

\* Aided by the Hartley Fund.

1. Stone, H. B., and Fitor, W. M.: *Tr. South. Surg. & Gynec. Ass.* 87:172, 1924.

2. Sherrington, C. E.: *Brain* 38:191, 1915.

any great difference from those operated on under ether and, indeed, in the instance already mentioned in which the intra-intestinal pressure was higher than usual during the first twenty-four hours and reached 36 cm. of water in six hours, ether had been used. Over this early period, there was no regularity of peristaltic action, as was found subsequently.

During the second twenty-four hours of obstruction, the sustained pressure remained between 6 and 8 cm. of water, while the degree of

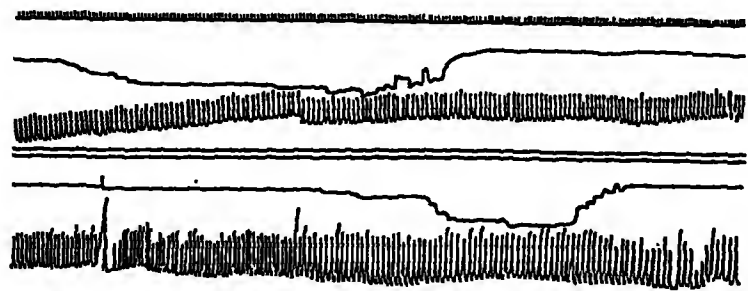


Fig. 2.—Tracing to illustrate the independence of the intra-intestinal pressure as compared with the respirations. Record of animal O. P. 15, in which obstruction had been produced in the lower part of the ileum for ninety-six hours; timer 3 seconds. A rise in the intra-intestinal pressure is represented on all the tracings by descent of the graph toward the bottom of the record.

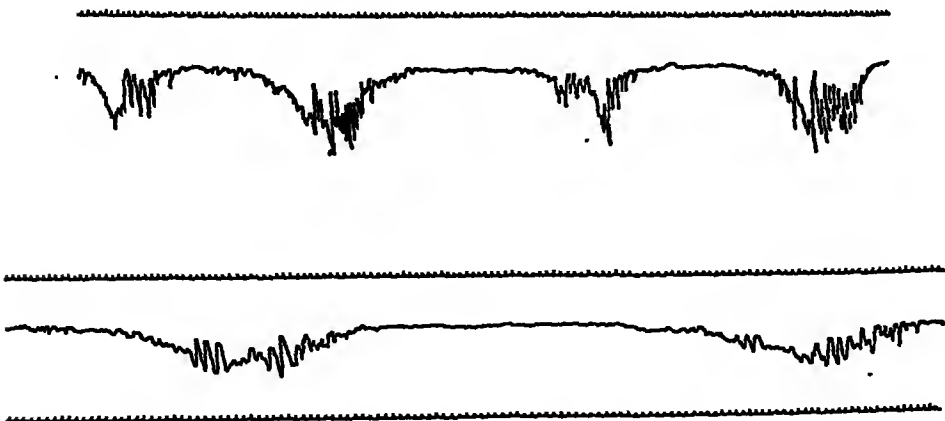


Fig. 3.—Graphic record obtained from one animal with a high intestinal obstruction and one with a low obstruction. The upper tracing is from animal O. P. 26, in which obstruction had been produced in the upper part of the jejunum for fifty-seven hours; the lower tracing is from animal O. P. 30, in which obstruction had been produced in the lower part of the ileum for fifty-two hours; timer 6 seconds.

pressure reached at the maximum of peristalsis rose considerably. In the dogs in which the high obstructions were produced, this pressure varied from 30 to 45 cm., while it generally took until the third day for the pressure in the dogs with low obstruction to reach the same-

motility of the bowel were obtained by a recording mercury manometer. Through a T-tube, a water manometer, 3 mm. in diameter, was attached in order to measure the lesser changes in pressure.

#### RESULTS

For the first twenty-four hours following operation, there was only a slight rise in the intra-intestinal pressure as a general rule, though in one case a considerable rise occurred within six hours. Usually

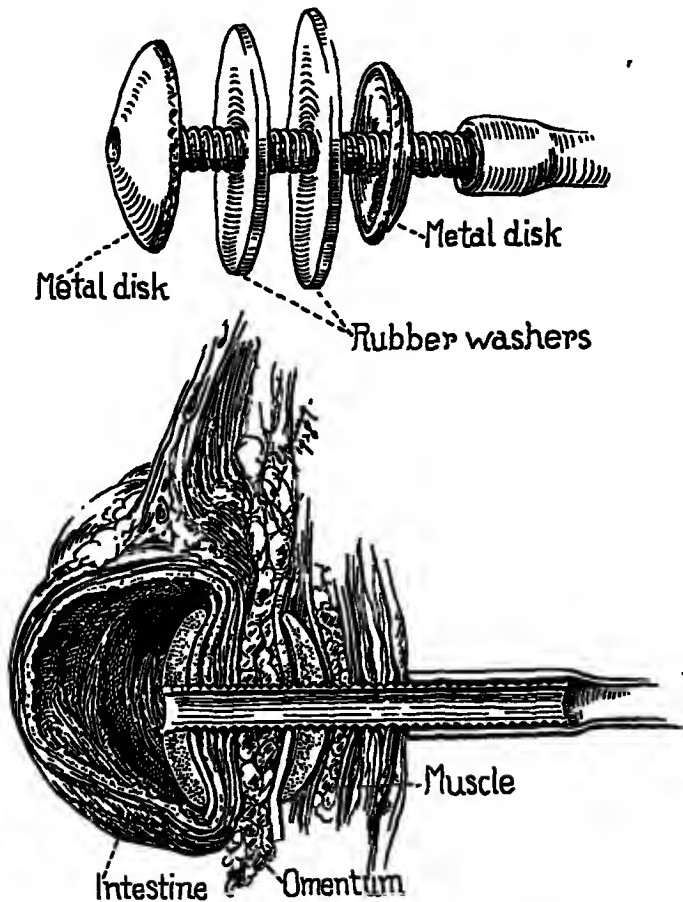


Fig. 1.—Drawing of apparatus described in technic is shown above; that of a cross-section of the apparatus in situ is shown below.

within twenty-four hours irregular peristaltic waves that reached a maximum of from 12 to 16 cm. of water were recorded. Between these there were inactive intervals during which the sustained pressure showed a gradual rise to 6 or 8 cm. As compared with the later observations, the bowel showed less activity during this early period probably owing, in the most part, to the operative trauma, the anesthesia and other factors. So far as the anesthesia was concerned, however, dogs in which obstruction was produced under procaine did not show



On the fourth day, the periods of increased pressure in the animals with high obstruction became less and less numerous, though the maximum level reached from 45 to 50 cm. of water. The sustained pressure began to decline, the toxicity of the animal increased quickly and death usually ensued about ninety-six hours after the obstruction. The dogs with low obstruction lived until the sixth or seventh day. The bowel showed good tone and considerable activity during the fourth and fifth days, after which fewer periods of increased pressure were noted and

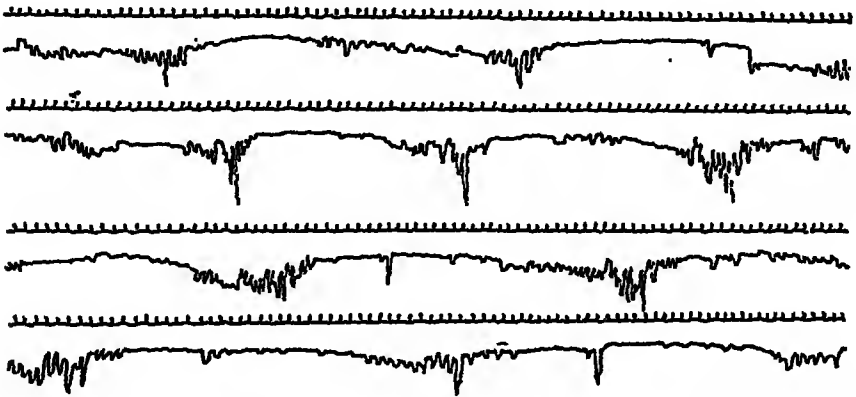


Fig. 6.—Record of animal O. P. 26 after obstruction had been produced for twenty-four hours; timer 6 seconds.

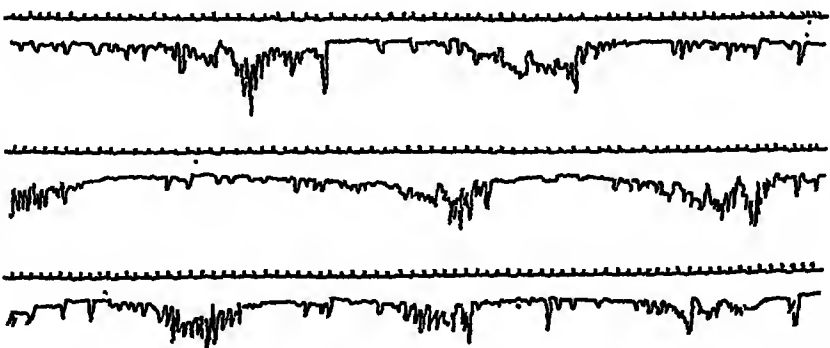


Fig. 7.—Record of animal O. P. 26 after obstruction had been produced for twenty-eight hours; timer 6 seconds.

the maximum level became less. The sustained pressure between these periods also diminished as the toxicity increased. During the twenty-four hours preceding death, the graphs showed slight undulations as the only evidence of intestinal motility.

The degree of pressure, then, within the lumen of the bowel in obstruction is greatly increased over the normal. The maximum levels in animals with high and low obstruction do not show great differences. The pressure rarely rises above 50 cm. of water, though in one isolated

level. The regularity of the peristaltic action became striking during this same interval. The periods of increased pressure in animals with high obstruction occurred about every third minute and lasted for about two minutes. In the animals with low obstruction, the regularity of action came on from forty-eight to seventy-two hours after the operation and the periods of increased pressure occurred every five to six minutes and lasted about three minutes. In other words, the periods of peristaltic action are more frequent in animals with high obstruction, and the graphic record obtained differed from that made in animals with

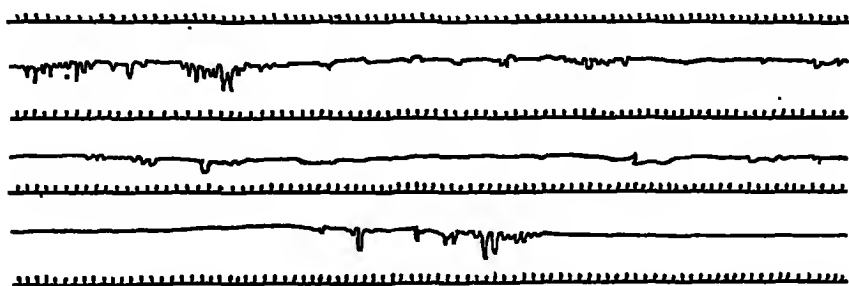


Fig. 4.—Graphic record from animal O. P. 26, after obstruction had been produced in the upper part of jejunum for four hours; timer 6 seconds.

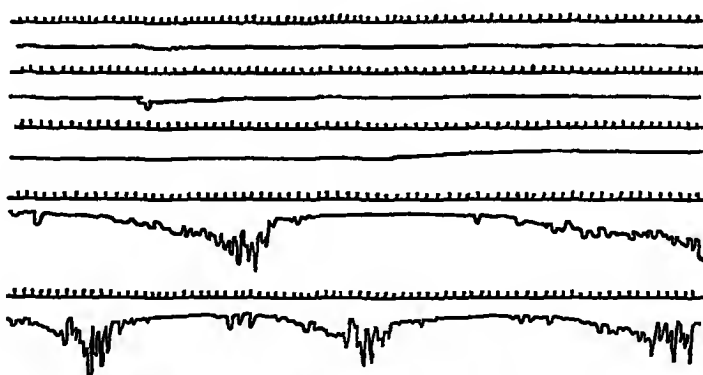


Fig. 5.—The upper three tracings show results in animal O. P. 26, after obstruction had been produced for ten hours; the lower two tracings, after twenty-two hours of obstruction; timer 6 seconds.

low obstruction in that a shorter time was taken for the pressure to reach its maximum. This is best shown in the kymographic records (fig. 3). The lower tracing, from an animal with low obstruction, shows a gradual increase in pressure with little irregularity until after the maximum is reached. The upper record, on the other hand, shows an abrupt or moderately abrupt rise in pressure with considerable irregularity. The fall in pressure in each case is much the same, showing marked evidence of peristaltic action, though somewhat more prolonged in the record made on animals with low obstruction.

instance a pressure of 58 cm. was reached. When accompanied by retching, vomiting or straining, the pressure is greatly increased and will reach above 100 cm.

In two instances, the intra-abdominal pressure was determined along with the intra-intestinal pressure. This was done by means of small soft rubber bags that were filled with water and placed within the abdomen; a connection was then made to a water manometer. A slight positive pressure was present when the animal was lying down; it measured from 1 to 4 cm. On deep inspiration, this level reached 8 cm. These variations were independent of the intra-intestinal pressure.

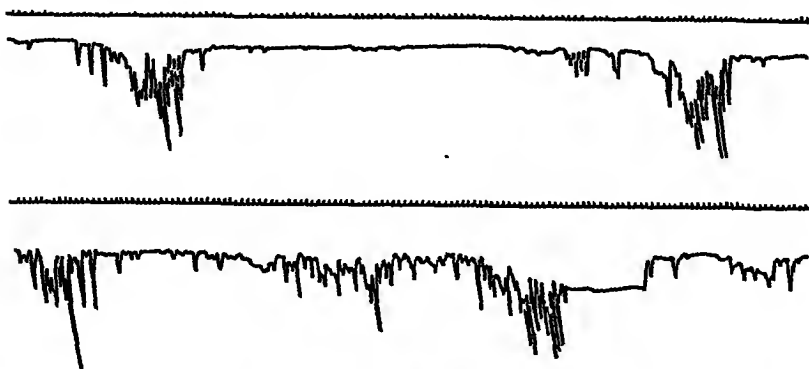


Fig. 11.—Record of animal O. P. 26 after obstruction had been produced for seventy-five hours; timer 6 seconds.

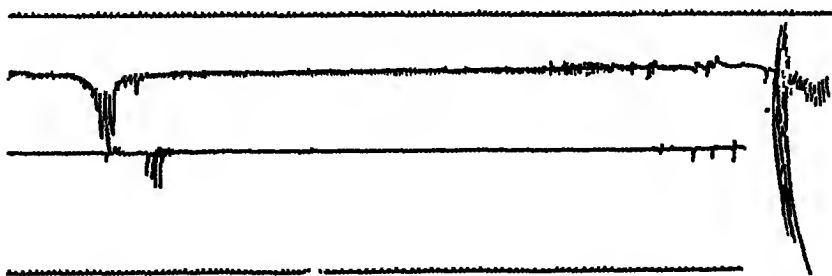


Fig. 12.—Record of animal O. P. 19 in which obstruction had been produced in the upper part of the jejunum for one hundred and thirty hours. Animal was moribund. Results show effect of respirations and vomiting; timer 6 seconds.

That the changes in the latter pressure are independent of the respirations is shown in figure 2. Extreme changes in intra-abdominal pressure, resulting from retching, vomiting and other conditions, however, are readily transmitted to within the lumen of the bowel (fig. 12).

In four instances, the pressure was measured within the lumen of isolated portions of the intestine. In three cases, these loops were made up of portions of duodenum and jejunum and in one instance of jejunum alone. Within the first twelve hours in all cases, the pressure

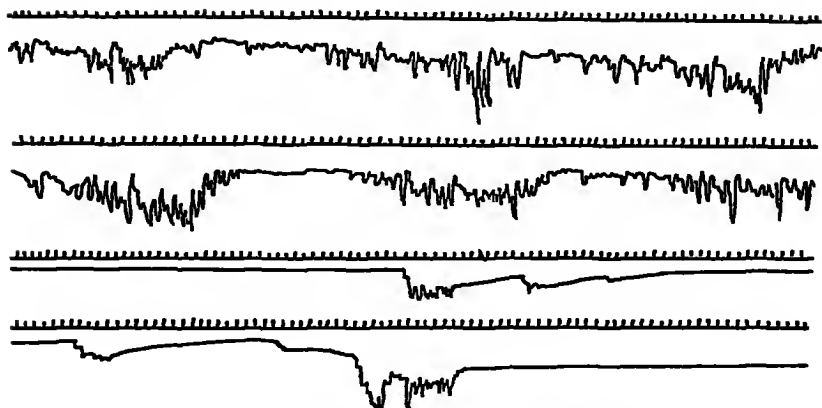


Fig. 8.—The upper two tracings show record of animal O. P. 26 after obstruction had been produced for thirty-three hours; the lower two tracings, after forty-eight hours; timer 6 seconds.

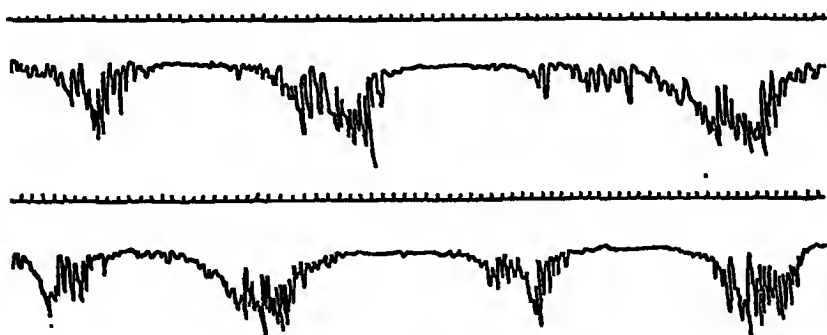


Fig. 9.—Record of animal O. P. 26 after obstruction had been produced for fifty-seven hours; timer 6 seconds.

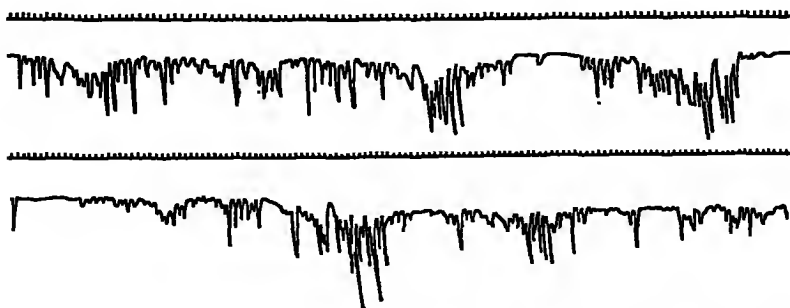


Fig. 10.—Record of animal O. P. 26 after obstruction had been produced for seventy-one hours; timer 6 seconds.



Fig. 16.—The upper tracing shows record from animal O. P. 17 after obstruction had been produced for ninety-six hours; the lower tracing, after one hundred hours; timer 3 seconds.



Fig. 17.—Record from animal O. P. 17 after obstruction had been produced for one hundred and twenty-four hours; timer 3 seconds.

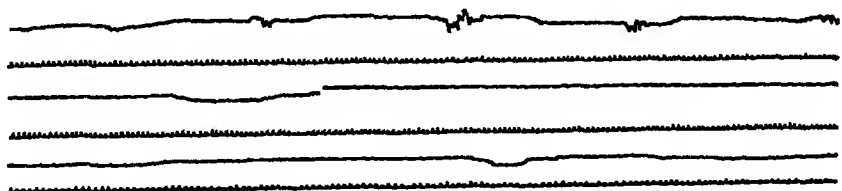


Fig. 18.—Record from animal O. P. 17 after obstruction had been produced for one hundred and fifty hours; timer 6 seconds.

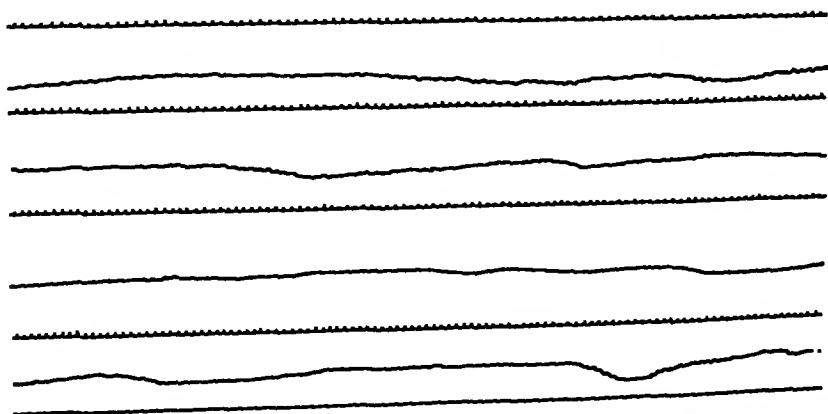


Fig. 19.—The upper two tracings show record from animal O. P. 17 after obstruction had been produced for two hundred and sixteen hours; the lower two tracings, after two hundred and twenty-one hours. The results show effect of fecal fistula; timer 6 seconds.

had risen to at least 30 cm. of water, and by twenty-four hours it had reached about 50 cm. The rhythmic periods of increased pressure were likewise present, and the sustained pressure between them showed a high tension, measuring from 16 to 18 cm. The sustained pressure

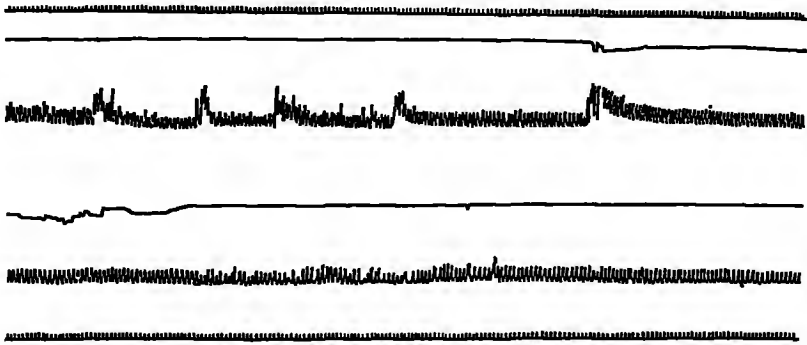


Fig. 13.—Graphic record from animal O. P. 17 in which obstruction had been produced in the lower part of the ileum for twenty-four hours. Respirations were recorded; timer 3 seconds.

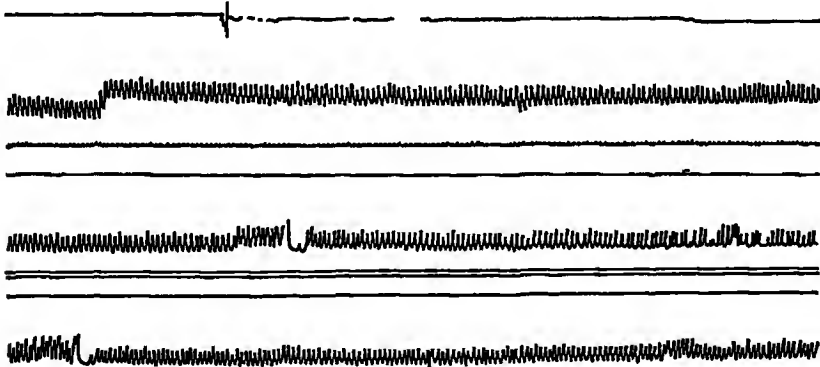


Fig. 14.—Record from animal O. P. 17 after obstruction had been produced for forty-eight hours. Respirations were recorded; timer 3 seconds.



Fig. 15.—Record from animal O. P. 17 after obstruction had been produced for seventy-six hours. Respirations were recorded; timer 3 seconds.

was maintained at a higher level than in the animal with simple obstructions and did not fall off until perforation occurred. The maximum pressure observed was 70 cm. of water. The length of life in these animals was from twenty-nine to forty-eight hours. Three died from general peritonitis resulting from a perforation of the loop at the

TABLE 2.—*Protocol of Dog O. P. 17*

Period of Observation	Hours Obstructed	Maximum-Minimum Pressure, Cm. Water		Notes
		Maximum	Minimum	
Feb. 10—11:00-12:00 a. m.	...	..	..	Operation; $\frac{1}{4}$ grain morphine; ether; obstruction lower part of ileum
Feb. 11—4:00-4:15 p. m.	4	14	10	
Feb. 11—11:00-12:00 a. m.	24	18	7	Fig. 13
Feb. 11—10:00-11:00 p. m.	35	18	7	
Feb. 12—12:00-1:00 p. m.	49	9	5	Fig. 14
Feb. 12—4:00-5:00 p. m.	52	12	8	
Feb. 13—11 a. m.-12:30 p. m.	72	36+	7	
Feb. 13—3:00-4:00 p. m.	76	44	5	Fig. 15
Feb. 14—10:30-11:15 a. m.	96	40	8	Fig. 16
Feb. 14—3:00-4:00 p. m.	100	28	8	Fig. 16
Feb. 15—12:00-1:00 p. m.	121	20	6	
Feb. 15—2:30-4:00 p. m.	124	30	6	Fig. 17
Feb. 15—8:30-9:30 p. m.	130	24	8	
Feb. 16—10:00-11:30 a. m.	144	16	6	
Feb. 16—3:45-5:15 p. m.	150	24	10	Fig. 18
Feb. 16—8:30-9:30 p. m.	154	18	10	
Feb. 17—11:00-12:00 a. m.	168	18	8	Fecal fistula
Feb. 17—4:30-6:00 p. m.	174	30	2	
Feb. 17—8:45-10:00 p. m.	177	16	8	
Feb. 18—2:50-4:00 p. m.	196	18	2	
Feb. 19—11:00-12:00 a. m.	206	14	10	Fig. 19
Feb. 19—5:00-6:00 p. m.	221	24	12	Fig. 19
Feb. 20—4:00-5:00 p. m.	244	No record		Fig. 20
Feb. 21—7:00 a. m.	...	..	..	Found dead; autopsy: general peritonitis

TABLE 3.—*Protocol of Dog O. P. 20*

Period of Observation	Hours Obstructed	Maximum-Minimum Pressure, Cm. Water		Notes
		Maximum	Minimum	
Feb. 16—11:00-12:00 a. m.	..	..	..	Operation; $\frac{1}{4}$ grain morphine; ether; isolated loop in duo- deno-jejunum; no anasto- mosis
Feb. 17—11:00-12:00 p. m.	12	30	12	Fig. 21
Feb. 17—10:00-11:30 a. m.	24	36	18	Figs. 21 and 22
Feb. 17—2:00-3:00 p. m.	27	44	14	Fig. 22
Feb. 17—5:00 p. m.	29	..	..	Dead; general peritonitis; per- foration of loop due to apparatus

TABLE 4.—*Protocol of Dog O. P. 26*

Period of Observation	Hours Obstructed	Maximum-Minimum Pressure, Cm. Water		Notes
		Maximum	Minimum	
Feb. 27—11:00-12:00 a. m.	..	..	..	Operation; procaine 2%; ob- struction in upper part of jejunum
Feb. 27—4:00-5:30 p. m.	4	17	5	5 cc. cold water injected into bowel; fig. 4
Feb. 28—9:30-10:30 p. m.	10	8	5	Fig. 5
Feb. 28—10:30 a. m.-1 p. m.	24	36	5	Figs. 5 and 6
Feb. 28—3:45-4:45 p. m.	28	30	6	Fig. 7
Feb. 28—9:00-10:00 p. m.	33	30	6	Fig. 8
Feb. 29—12:00-1:00 p. m.	48	28	10	Fig. 8
Feb. 29—3:00-4:30 p. m.	51	30	6	
Feb. 29—8:30-9:30 p. m.	57	54	6	Fig. 9
March 1—10:00-11:00 a. m.	71	54	6	Fig. 10
March 1—3:00-4:00 p. m.	75	58	6	Fig. 11
March 2—7:00 a. m.	..	..	..	Found dead; autopsy showed local adhesions only

antimesenteric border. In the fourth there was a leak about the apparatus and peritonitis resulted.

In the animals with simple obstruction, perforation or gangrene of the antimesenteric border was not encountered, as in the experiment on animals in which a loop was made. This is of interest, for in the

TABLE 1.—*Data for Dogs Used in Experiment*

No.	Serial No.	Anesthetic	Site of Obstruction	Duration of Life, Hours	Cause of Death
1	O.P. 6	Morphine and ether	Upper part of jejunum	56+	Toxemia and general peritonitis
2	O.P. 8	Morphine and ether	Lower part of ileum	78+	Toxemia and local peritonitis
3	O.P. 9	Morphine and ether	Middle small bowel	102+	Toxemia and distemper
4	O.P. 10	Procaine	Upper part of jejunum	100+	Toxemia and local peritonitis
5	O.P. 11	Procaine	Middle small bowel	53+	Toxemia and local peritonitis
6	O.P. 12	Procaine	Lower part of ileum	77+	General peritonitis and distemper
7	O.P. 13	Morphine and ether	Middle small bowel	103+	Toxemia and local peritonitis
8	O.P. 14	Morphine and ether	Upper part of jejunum	76+	Toxemia and local peritonitis
9	O.P. 15	Morphine and ether	Lower part of ileum	121	Toxemia and general peritonitis
10	O.P. 16	Morphine and ether	Lower part of ileum	75+	Toxemia and general peritonitis
11	O.P. 17	Morphine and ether	Lower part of ileum	221+	Toxemia and general peritonitis
12	O.P. 18	Morphine and ether	Middle small bowel	60	Toxemia and general peritonitis
13	O.P. 19	Morphine and ether	Upper part of jejunum	130+	Toxemia and local peritonitis
14	O.P. 20	Morphine and ether	Isolated loop in duodenojejunum	29	General peritonitis
15	O.P. 21	Morphine and ether	Isolated loop in jejunum	48	General peritonitis
16	O.P. 22	Morphine and ether	Upper part of jejunum	56	Toxemia and general peritonitis
17	O.P. 23	Morphine and ether	Isolated loop in duodenojejunum	54+	General peritonitis
18	O.P. 24	Morphine and ether	Isolated loop in duodenojejunum	45	General peritonitis
19	O.P. 25	Procaine	Lower part of ileum	29	General peritonitis (chloroformed)
20	O.P. 26	Procaine	Upper part of jejunum	76+	Toxemia
21	O.P. 27	Procaine	Lower part of ileum	140+	Toxemia
22	O.P. 30	Morphine and ether	Lower part of ileum	216	Chloroformed (fecal fistula)

latter instance we find that the pressure rose more quickly and reached a higher level, while the sustained pressure between the periods of increased tension was more than twice that found in the animals in which simple obstruction was produced.

Most of the animals, as is shown in table 1, died of a complicating peritonitis. There can be little doubt that this would materially affect the intestinal motility and probably cause the fall in pressure that is



graph was taken within two or three hours of death while the animal was moribund, but it shows what we found the more common record of the intestinal motor activity before death. Without a complicating peritonitis, then, we feel all our graphs would show more evidence of peristalsis than they have done within twenty-four hours of death, but that even without peritonitis the pressure falls and the motility becomes less with the increasing toxemia of obstruction.

Figures 19 and 20 are of interest as they show the changes that come from the development of a fecal fistula. The drainage in this case was not sufficient to empty the obstructed bowel, so that a pressure was kept above the normal but below that within an obstructed bowel without a fistula. A well marked change in the character of the graphs is noted.

#### SUMMARY

The conclusions that follow from these experiments seem to show that in small dogs with simple obstruction the intra-intestinal pressure is maintained at a level (from 6 to 8 cm. of water) about twice that of the normal maximum (from 2 to 4 cm. of water). While the bowel is active, the pressure rises to ten or fifteen times the normal (from 30 to 60 cm. of water).

What we consider a fairly exact conception of the type and magnitude of the intestinal motility in obstruction throughout its course is shown in the accompanying tracings. Three periods may be roughly distinguished. The first, which embraces the twenty-four hours following obstruction, shows little change from the normal. The second period shows a rise in the basic or sustained pressure with marked peristalsis and a great increase in the intra-intestinal pressure generally. The third or terminal phase shows a falling pressure and a decrease in the peristaltic activity.

The fact that periods of violent peristalsis come on earlier and are more frequent in animals with high obstruction than in those with low obstruction may have some clinical value in helping one to locate the site of obstruction.

In experiments in which an isolated loop was made, the degree of pressure reached (70 cm. of water) is much greater than that in dogs with simple intestinal obstruction.

so marked during the final twenty-four hours. That this is the case might be concluded from the graphs obtained from the animals with high obstruction that are shown in figures from 4 to 11. The last graph was obtained within sixteen hours of death, and the intestinal motility, as is shown by the records, was nearly as active as at any earlier period.

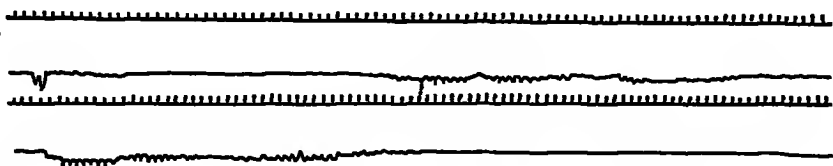


Fig. 20.—Record from animal O. P. 17 after obstruction had been produced for two hundred and forty-four hours; timer 6 seconds.

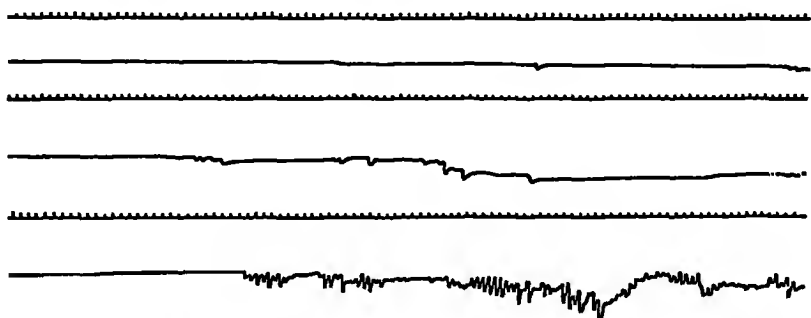


Fig. 21.—The upper two tracings show record from animal O. P. 20 after isolated loop had been produced in the duodenojejunum for twelve hours; the lower tracing, after twenty-three hours; timer 6 seconds.

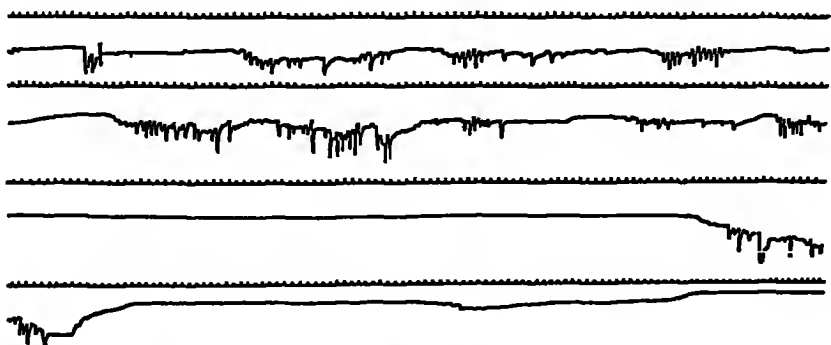


Fig. 22.—The upper two tracings show record from animal O. P. 20 after isolated loop had been produced for twenty-four hours; the lower two tracings, after twenty-seven hours; timer 6 seconds.

Autopsy did not reveal general peritonitis and no local adhesions or exudation beyond what one might expect after such manipulation. Death was thought to be due, therefore, in most part to the toxemia of obstruction. Figure 12 was obtained from another animal with high obstruction that, as shown at autopsy, had general peritonitis. The

rachitic genu varum and valgum represent a regressive phase or variation in the development of growth of the skeleton of the lower extremities. In the new-born child, the knee is in a position of flexion, outward rotation and lateral declination in relation to the general alinement of the leg. Boehm has shown from studies of many children and of anatomic specimens that during the first five years of growth the alinement of the leg changes, the knee rotating slightly inward, losing its flexion and assuming a slight medial declination. However, variations may occur and in certain persons these may be of a regressive type, leading eventually to the formation of genu valgum or varum. Static and mechanical forces resulting from weight bearing were regarded by Boehm as important, not as primary factors in influencing the development of the deformities but as occurring secondarily after the variation in the anatomic development of the leg has been produced.

#### RICKETS

*Historical.*—Writing of the history of the knowledge of rickets, Foote<sup>3</sup> stated that when Whistler published his thesis in 1645, and Glisson his book in 1650, it was called an entirely new disease. According to present theories of cause, there is no reason to suppose that the disease did not exist before 1650. Swaddling was a method employed by ancient peoples to prevent the development of deformities. Soranus of Epiphysus apparently wrote about the disease in the second century A. D. The author has observed in the Army Medical Museum at Washington the skull of a pre-Columbian Peruvian boy with typical rachitic changes. Between 1450 and 1500, Bruges described the disease in England. Portraits by Lochner, Strigal, Bergmaier and others show rachitic changes. Foote concluded that the disease undoubtedly existed at all times and periods.

*Sunshine and Skyshine.*—Tisdall and Brown<sup>4</sup> made a study of the effect of seasonal variation on the antirachitic value of sunshine in the latitude of Toronto. Experiments were conducted on albino rats which were kept on a constant rachitogenic diet. The rats were exposed two hours daily and the results appraised from study of roentgenograms and analysis of the calcium and phosphorus in the blood and bone. The authors concluded that the sun's rays in the vicinity of Toronto have slight but definite antirachitic effect, and that there is a sharp increase in the antirachitic effect of sunshine, beginning in March. In April and May, the antirachitic effect is approximately eight times as great as in

3. Foote, J. A.: Evidence of Rickets Prior to 1650, *Am. J. Dis. Child.* **34**: 443 (Sept.) 1927.

4. Tisdall, F. F., and Brown, A.: Seasonal Variation of Antirachitic Effect of Sunshine, *Am. J. Dis. Child.* **34**:721 (Nov.) 1927.



that twice as many rats which had been exposed to the sun survived intraperitoneal infection as those which had not been exposed.

[Ed. NOTE.—The articles summarized reporting the results of investigations of the antirachitic properties of radiation are only a few of a great many dealing with different phases of the same general subject that have been published in the last few years. Little by little the knowledge of the action and effects of radiation is being increased, and already a certain amount of order has emerged from what a short time ago was chaos. While the subject is being approached chiefly from its relation to rickets, the orthopedic surgeon cannot lose sight of the larger bearing of radiation in relation to the function of bone and the treatment of bone diseases in general. It is reasonable to suppose that increase of knowledge concerning radiation in rickets may also have a bearing on the employment of light therapy in other conditions.]

*Rachitic Deformities of the Lower Extremities.*—Moore<sup>8</sup> made a study of rickets in the lower extremities. He found that in normal legs the approximating epiphyseal plates of the femur and tibia are parallel and that when the inner borders of the feet are parallel both the knees and the ankles are in contact. In a typical example of rickets, he found that the epiphyseal lines of each knee, if extended, would meet at an acute angle. With the planes of the lower femoral and upper tibial epiphyses coming together on the outside, knockknee would naturally result. The vacant space between the epiphyses in the open part of the angle gradually fills up with calcified bone and new epiphyseal planes are formed, parallel to each other but at an abnormal angle to the long axis of the diaphyses of both the tibia and the femur. The author stated that until such a joint becomes fixed in a normal or a valgum or varum position a decided lateral mobility is demonstrable. This exaggerated mobility of the knee is often the first sign of rickets in the leg. A normal knee gives a lateral movement of 3 cm. or less as measured at the heel, regardless of the length of the leg. A knee mobility arthrometer was devised so that mathematically accurate measurements could be obtained each month and become an index of the amount of lateral mobility of the knee. According to the author, this index may be used to determine whether or not genu valgum or varum is imminent. After such a deformity has developed, its value lies in determining whether the joint has become too set to be capable of correction by brace treatment.

#### DISTURBANCES OF DEVELOPMENT AND GROWTH

*The Ovary in Osteomalacia.*—Writing on the relation of the ovary to osteomalacia, Fraser<sup>9</sup> stated that a close relationship between the ovary, pregnancy and osteomalacia has been recognized since Fehling

8. Moore, Ulysses C.: J. Bone & Joint Surg. 10:96 (Jan.) 1928, no. 1.

9. Fraser, J. R.: Am. J. Obst. & Gynec. 14:697 (Dec.) 1927.

December, January and February. These results agree with those of Dorno, who found the ultraviolet content of midday sun in the Alps in January only 10 per cent as great as in July.

Similar methods were employed by the same authors<sup>4a</sup> in testing out the antirachitic action of skyshine. The rats were exposed on the shady side of the roof. The authors concluded that the effect of skyshine is from about one-half to two-thirds as great as that produced by sunshine.

Hess and Anderson,<sup>5</sup> by an improved technic, showed that ultraviolet radiation with rays shorter in length than those of sunshine is more potent in healing rickets than the effective area of solar rays. The effective band comprises the waves between 290 and 313 millimicrons. The studies brought out the fact that the area of specific solar radiation is markedly circumscribed, and that a difference of a few millimicrons or millionths of a millimeter determines whether or not waves are effective. During the winter months when the shorter ultraviolet rays do not reach the earth and the longer ones are less intense, the width of the antirachitic zone of sunlight is only about 5 millimicrons. These observations emphasize the danger of the small band of specific radiation being filtered from the atmosphere by moisture, dust, smoke, and other foreign substances.

Tisdall and Brown<sup>6</sup> tested the antirachitic value of the sun's rays when passed through various special window glasses. These included Vitaglass, Vicray glass and Corning glass. They concluded that the effect obtained was from 25 to 50 per cent of that obtained without the use of glass. An obvious difference could not be detected between the three glasses. The antirachitic effect of sunshine which had passed through ordinary glass was shown to be negligible except immediately adjacent to the window. The authors stated that with any type of glass it is necessary to employ the direct rays of the sun in order to receive much benefit, and that in winter the use of special glass is probably of little benefit.

Robertson<sup>7</sup> reported an investigation of the effect of exposure to the sun on susceptibility of rachitic rats to infection. The organism used as the infecting agent in the experiments was a gram-negative bacillus isolated from the nose of a normal rat. The author showed

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4a. Tisdall, F. F., and Brown, A.: Antirachitic Effect of Skyshine. *Am. J. Dis. Child.* **34**:737 (Nov.) 1927.

5. Hess, Alfred F., and Anderson, William, T.: Antirachitic Activity of Monochromatic and Regional Ultraviolet Radiations, *J. A. M. A.* **89**:1222 (Oct. 8) 1927.

6. Tisdall, F. F., and Brown, A.: Antirachitic Effect of the Sun's Rays Through Various Special Glasses. *Am. J. Dis. Child.* **34**:742 (Nov.) 1927.

7. Robertson, E. C.: *Canad. M. A. J.* **17**:1033 (Sept.) 1927.

do not have blue sclerae do not transmit the disease to their offspring. Little is known concerning treatment, and all present methods are of practically no avail.

*Bone Tissue in Conditions of Circulatory Disturbance.*—Mueller<sup>12</sup> studied bone tissue from persons with disturbed circulation, such as occurs in arteriosclerosis, and found definite structural changes. The intermediary lamellae showed areas of necrosis, while the lamellar systems surrounding central vessels and marrow spaces were essentially normal. The necrotic areas were found only in the compact bone and were totally lacking in the spongy bone. In senile bone without accompanying arteriosclerosis necrotic areas were not seen. Bone proliferation and evidence of reaction such as are usually seen in the vicinity of necrotic bone areas were not seen in the specimens of bone from patients with circulatory disturbance.

#### SCOLIOSIS

Lucas<sup>13</sup> stated that while he considered the treatment of structural scoliosis still far from satisfactory, he had employed Steindler's method with good results. By this method the proper body alinement is maintained by the formation of compensatory curves above and below the primary curve. Direct force is not applied to the primary curve. The first stage of the treatment lasts from one to two months and consists of gymnastics for stretching and loosening the spine and of extension on a Bradford frame. Extension is obtained by applying about 10 pounds to the head and from 30 to 40 pounds to the pelvis. In case there is much deformity of the chest, blowing on Wolff's bottles is prescribed. The second stage is one of fixation and lasts from two to three months. A series of plaster jackets is applied, the child being suspended with the head sling. The arm on the concave side is abducted and the hip on this side adducted. If at the end of this time the body alinement is good, the spine stable with good compensatory curves and the muscles sufficiently strong, the child is sent home in a brace. If the spine is unstable, a fusion operation is performed by Hibbs' method. After operation, the child is kept recumbent for three months with plaster fixation; then a brace is worn for one year longer.

Summarizing an article on scoliosis, Ober and Ghormley<sup>14</sup> stated that functional and mild structural curves can be managed by simple corrective exercises and apparatus. Operative measures are to be recommended in adult patients whose spines are not already fixed by

12. Mueller, W.: Beitr. z. klin. Chir. 138:494, 1926.

13. Lucas, L. S.: Northwest Med. 26:588 (Dec.) 1927.

14. Ober, Frank R., and Ghormley, Ralph K.: Scoliosis, J. A. M. A. 90:361 (Feb. 4) 1928.

introduced castration in 1887. Experimental work has shown that the ovaries exert a marked influence on phosphorus metabolism. Blair Bell mentioned a 50 per cent reduction in excretion of calcium after ovariectomy. Fraser described the changes noted in an ovary removed in midpregnancy from a patient with well marked osteomalacia. Not only the cortex but the entire ovary showed a marked hyperplasia of the glandular and interglandular tissue. There was a general venous congestion and widespread formation of follicles. All stages of maturation of the follicles were seen. Many atretic follicles were present, many of them cystic and with proliferation of the thecal cells. There were more large vessels present than is usually found, particularly in the medulla. This may merely represent a further stage of what normally occurs during pregnancy. The author expressed the belief that the ovary plays a part in osteomalacia because of the therapeutic benefit following castration, the frequent occurrence and aggravation of the disease with pregnancy, the high degree of fertility in this disease, and the changes which the author has described.

*Osteogenesis Imperfecta.*—Welz and Lieberman<sup>10</sup> reported the occurrence of osteogenesis imperfecta in single ovum twins. The first infant died in nine hours and the second in fourteen hours. The blood calcium in the mother was 8.9 mg. per hundred cubic centimeters of blood, and in the second infant was 10.1 mg. per hundred cubic centimeters of blood. The Wassermann reaction was negative. Roentgen-ray examination of the second infant showed fractures in nearly every bone in both the upper and the lower extremities, in various stages of healing, also healed fractures of most of the ribs on both sides. Marked deformities were present in both femora. There was no evidence of injury to the spine. The clavicles were not broken. The epiphyses of the tibia showed a dense straight line of bone deposit. Roentgen-ray examination of the first infant showed an almost identical appearance. In this case, however, the clavicles were broken.

*Brittle Bones and Blue Sclera.*—Colby<sup>11</sup> reported that there had been brought to his attention three members in one family with brittle bones and blue sclerae. One child had blue sclerae but had not had any fractures. Another child, a girl, aged 5 years, had had four previous fractures from slight trauma. Discussing the disease in general, the author said that it is usually called osteogenesis imperfecta and that it is characterized by brittle bones, blue sclerae, deafness and hypermobility of the joints. It was first described by Von Ammon in 1839. It is transmitted by direct inheritance, and children of affected parents who

10. Welz, W. E., and Lieberman, B. L.: *Am. J. Obst. & Gynec.* 14:49 (July) 1927.

11. Colby, F. G.: *Southwestern Med.* 11:36 (Aug.) 1927.



there is no logical reason for the transmission of pelvic pain into the lower lumbar and sacro-iliac regions.

*Etiologic Factors in Sciatic Scoliosis.*—That fecal retention in the large bowel may be an etiologic factor in the production of certain disease symptoms, particularly of the syndrome of the so-called sciatic scoliosis, has impressed Osgood<sup>17</sup> from his experience in treating some of these patients. He has made a detailed report of six patients showing this symptom-complex. The duration of the symptoms was very long. All of the usual methods of orthopedic treatment had been tried without avail. Relief was finally obtained from measures directed toward the correction of colonic stasis and fecal retention, such as intestinal massage and colonic irrigations.

*Abnormalities of the Lumbar Spine.*—O'Reilly<sup>18</sup> continued his investigations of the anatomic abnormalities of the lower spine. He found them present in a high percentage of cases. In a series of 100 roentgenograms, some abnormality was present in 33 per cent, and in an examination of dried bones, abnormalities were found in 17 per cent. The most common abnormality was sacralization of the transverse process of the fifth lumbar vertebra, either fused to the sacrum or articulating with it. The author pointed out the fact that the presence of abnormalities in the so-called normal back frequently leads to legal complications after an injury. In order to prevent this and to protect the workman with a potentially weak back from serious strain, O'Reilly proposed that all workers whose occupations might result in back strain should have a roentgenogram of the spine made before being employed.

*Operation for Extra-Articular Fusion of the Sacro-Iliac Joint.*—An operation for extra-articular fusion of the sacro-iliac joint was reported by Campbell.<sup>19</sup> The essential feature is the transplantation of a portion of the posterior crest of the ilium into the posterior sacro-iliac fossa and packing it about with bone chips. The postoperative treatment consists of recumbency on a Bradford frame for a period of six weeks. Thus far the author has performed the operation on seven patients. Of these, five are apparently well, and in the other two the operation has been performed too recently to permit an estimation of the result.

[Ed. NOTE.—This operation appears somewhat similar to one originated by Dr. E. G. Brackett about fifteen years ago. He used a transplant from the tibia, while Campbell employed a bone graft from the crest of the ilium. We believe that Brackett has since abandoned his operation in favor of Smith-Petersen's operation.]

17. Osgood, Robert B.: *J. Bone & Joint Surg.* 9:667 (Oct.) 1927.

18. O'Reilly, Archer: *Abnormalities of Lower Part of Back*, *J. A. M. A.* 89: 1128 (Oct. 1) 1927.

19. Campbell, W. C.: *Surg. Gynec. Obst.* 45:218 (Aug.) 1927.

nature and who are doomed to wear a jacket for life. Fusion operations should not be performed on growing children except in paralytic conditions and then only in case of severe deformity which cannot be held by other measures. In the authors' opinion, the principal indications for operative treatment are: (1) rapid increase of the curve; (2) signs of general debility or ill health; (3) rib pressure with intercostal or pelvic pain, and (4) inability to hold the curve in persons with infantile paralysis. The first three indications are for adults; the fourth is for children or adults.

[ED. NOTE.—We are in agreement with the opinions of the last authors but would supplement their operative indications by adding cases in which the curve is the result of an anatomic defect such as a wedge-shaped dorsal vertebra. Experience indicates that such curves increase with the growth of the patient irrespective of all corrective measures except fusion operations, and sometimes even in spite of them.]

#### PAIN IN THE BACK

*Abdominal Symptoms Associated with Chronic Strain of the Spine.*—Carnett<sup>15</sup> expressed the belief that midline abdominal pain may be caused by chronic strain of the lumbar spine and sacro-iliac joints. He observed the condition repeatedly. It is associated with an increased lumbar lordosis and increased dorsal kyphosis. Midline tenderness is found sharply limited to the area of the intra-abdominal portion of the vertebral bodies, and all aspects of the vertebrae and intervertebral disks that are accessible to palpation are uniformly tender. The majority of the patients who exhibit midline tenderness also have an isolated area of tenderness in each iliac fossa over the superior portion of the sacro-iliac joint. The midline tenderness has often been considered aortic tenderness and also sometimes mistaken for tenderness due to appendicitis. In many of the patients with exaggerated lumbar lordosis, the dominant symptoms are those of irritation of the intercostal nerves, which is more or less widespread but is manifested mainly by pain and tenderness over the abdomen, particularly in the right lower quadrant.

*Pain in the Lower Part of the Back in Connection with Pelvic Disorders.*—The various causes of backache have been considered by Kreuscher,<sup>16</sup> and he has pointed out the infrequency of the production of this symptom by gynecologic disorders. His chief argument against any relationship between uterine conditions and pain in the back is that the innervation of the uterus is derived from the pelvic plexus, the ovarian plexus and a few filaments from the sacral nerves. Consequently,

15. Carnett, John Berton: Ann. Surg. 85:509 (April) 1927.

16. Kreuscher, P. H.: Surg. Gynec. Obst. 45:482 (Oct.) 1927.

important, the author stated, to observe whether the pressure to be relieved is due to the supernumerary rib or to the normal first rib.

*The Articular Mechanism of the Diarthroses.*—Walmsley<sup>22</sup> reported the results of his study of the articular mechanism of the diarthroses. He stated that at the majority of the diarthroses two functions are equally to be served: (1) the function of weight transmission, which is accomplished in only one position and to secure which there are the articular mechanisms, and (2) the function of movement, during which the surfaces of the elements are moved on one another and maintained in their relations to one another by the mechanisms of movement, which are the related muscles. Each function has its own mechanism. Walmsley said that there is one aspect of mechanism of the joints that has not always been taken into account in descriptions of function of the joints and, in fact, is by no means universally admitted, namely, "The definite and nonreciprocal shape of the joint surfaces which determines that they are in full congruence only in the positions in which they transmit weight and are incongruent in all other positions. . . . At the hip joint as the limb moves toward extension, and materially assisted by the anterior inclination of the neck of the femur, the capsule is progressively twisted and shortened, and, as it were, guides the head of the bone like a screw into its socket until at the position of full extension (about fifteen degrees beyond the vertical) the capsule is taut, the head of the bone is screwed home, the surfaces are fully congruent, and further movement of a larger on to a smaller surface is impossible."

[ED. NOTE.—The author brings out a point in reference to the mechanism of the hip that is most important in the reduction of fractures of the hip, namely, the screwing home action of the motion of extension. To approximate the fragments, it is necessary not only widely to abduct and internally rotate the hip, but also to extend it.]

#### ARTHRITIS

*General Articles.*—Pemberton<sup>23</sup> stated his conclusions regarding chronic arthritis after a clinical and biochemical investigation of 1,200 cases. He considered the division of the cases into proliferative and degenerative types the simplest and best classification. He thought that the rôle of focal infection in the production of the disease is over-emphasized. He noted evidence of an intimate relationship between arthritis and the nervous system in the frequent occurrence of par-esthesia and other vague nervous sensations. In all the large groups so

22. Walmsley, Thomas: *J. Bone & Joint Surg.* 10:40 (Jan.) 1928.

23. Pemberton, Ralph: *Michigan State M. J.* 26:599 (Oct.) 1927.

MECHANICAL DISTURBANCES, ANATOMIC INVESTIGATIONS,  
CERVICAL RIBS

*Cervical Ribs.*—From a study of patients with cervical ribs treated at the Mayo Clinic, Adson and Coffey<sup>20</sup> drew the following conclusions: In about 55 per cent of the cases cervical ribs do not cause any symptoms, and patients in whom the condition is discovered purely by accident ought not to be informed of it, as this knowledge is apt to give rise to neuroses with symptoms referable to the rib. The surgical indications depend on the degree and the character of the incapacity produced by the presence of pain, hyperesthesia, anesthesia and circulatory disturbance. Surgical treatment ought not to be advised for the relief of mild, indefinite pain in the neck and shoulder. The authors consider that the anterior approach and tenotomy of the scalenus anticus muscle are preferable to the transcervical approach and resection of the cervical rib, since the same relief is obtained, the procedure is less formidable and postoperative numbness in the arm and palsy of the brachial plexus are avoided.

[ED. NOTE.—It is to be remembered that symptoms apparently due to cervical rib may often be relieved by orthopedic treatment directed toward improving posture and relieving irritation and mechanical disturbances of the cervical spine. Such treatment ought to be given a trial before operation is resorted to. As far as not telling the patient of the accidental discovery of a symptomless cervical rib is concerned, we do not agree with the authors. Leaving aside the ethical question which is here raised, we believe there are few patients injured by the frank discussion of the condition found on examination, provided that the harmlessness of the condition is explained.]

*Pressure on the Brachial Plexus by the Normal First Rib.*—Brickner<sup>21</sup> made a study of patients with symptoms of pressure on the brachial plexus caused by a normal first rib. He reported six cases of his own. In the less severe cases the symptoms are pain in the arm, paresthesia and other phenomena. These may be relieved by elevating the shoulder and by exercising the trapezius to keep the shoulder elevated. Three of the author's cases were of this type, the symptoms probably being due to the dragging of the brachial plexus over the first thoracic rib. In the more severe cases all the phenomena of pressure by a cervical rib are produced by the pressure of an abnormal or even a normal first thoracic rib. Several of the patients required operative treatment and were relieved by resection of the first rib. When an operation is performed on a patient with a cervical rib, it is

20. Adson, Alfred W., and Coffey, Jay R.: *Ann. Surg.* 85:839 (June) 1927.

21. Brickner, Walter M.: *Ann. Surg.* 85:858 (June) 1927.

Bacterial infection may have provided the final thrust which started the disease. In the author's opinion, such patients are never cured or the condition arrested by any single line of attack such as removal of foci of infection. Hypertrophic arthritis presents an almost opposite picture. The patients are usually of the thickset type. Bacterial infection is not the cause of the condition, and it cannot be cured by removal of the local foci. Schauffler expressed the view that in the infectious type removal of the foci of infection and the administration of iodoxybenzoate sodium or ammonium intravenously with careful technic is the most efficient treatment in subacute and chronic cases.

*Etiology.*—Cecil<sup>25</sup> discussed the etiology of chronic arthritis. His views may be summarized as follows: In infectious arthritis, the inciting cause is focal infection. The predisposing causes are old age, overweight, faulty posture, occupation, physical defects and exposure. In metabolic arthritis or gout, the exciting cause is uric acid. The predisposing cause is purine diet and heredity.

Jones<sup>26</sup> expressed the belief that the lesions in the joints of persons with osteo-arthritis are end-results which may be arrived at by a variety of pathologic states. Quantitative and qualitative alterations, in internal secretions led to disturbances in the normal current of metabolism. It is the opinion of the author that the disease is due to nutritional alterations in the articular structures. They are not inflammatory. Hypothyroidism is common in the disease. Trauma is often the inciting cause. There are two stages in the history of osteo-arthritis. The primary stage is marked by symptoms of villous overgrowth. The later or terminal is the osteo-arthritic phase. Static factors are important. The disease should be recognized in the initial stage. Roentgen-ray examination is usually negative in the early stage.

*Relation of Surgical Pathologic Conditions of the Right Lower Quadrant to Chronic Arthritis.*—Discussing the relationship of surgical pathologic conditions of the right lower quadrant of the abdomen to chronic arthritis, Taylor<sup>27</sup> described the lesions he had been able to demonstrate in patients affected with this disease by roentgen-ray examinations after the patient had ingested an opaque meal. The author's studies and observations are of interest in suggesting the amount of information that may be obtained in regard to the presence and causes of intestinal stasis by thorough work and enthusiastic cooperation between the roentgenologist and the clinician. They point to an association between intestinal conditions and polyarthritis.

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25. Cecil, R. L.: *Southern M. J.* 21:20 (Jan.) 1928.

26. Jones, A. B.: *M. J. & Rec.* 126:557 (Nov. 2) 1927.

27. Taylor, Raymond G.: *J. Bone & Joint Surg.* 10:62 (Jan.) 1928.

far studied, women predominated. In the group studied by the author, exposure played an important rôle. Anemia also occurred more frequently in the women who had arthritis. Pemberton's biochemical studies showed that the nitrogenous metabolism is normal in the disease: hence, there is no reason to restrict proteins in the diet. On the other hand, evidence of slowed sugar metabolism has been frequently noted, which the author explained on the basis of poor circulation with less oxygen available for the consumption of the sugar. The blood does not appear to reach the tissues adequately. In a study of the red blood count in arthritis, it was found that the first drop of blood had a lower count than the fourth or fifth, which is the reverse of normal. By studying the capillaries by Lombard's method, the author found them to be less well filled with blood than normal. The capillaries appeared to be contracted. Because of this observation the author experimented with the administration of sodium nitrate in persons with arthritis, but is not yet ready to evaluate the therapeutic efficiency of this measure. The author observed proliferative changes in the patellae of dogs after ligation of the blood vessels to the patella. Pemberton stated that with the exception of removal of foci of infection, vaccines and nonspecific protein therapy, the measures used achieve their effect through their influence on blood flow or metabolism, or both. Arsenic is of value in the treatment of the anemia. Colonic irrigation and colonic massage are sometimes helpful, but in the author's opinion regulation of what is taken into the mouth is of more value. He considered the development of the mechanistic conception of disease and orthopedic treatment based on it a distinct advance. In conclusion, the author attempted to answer the question of what avail is treatment. Of 188 patients who were followed, 24 per cent were completely cured and 73 per cent were definitely improved. He expressed the opinion that most of the present sufferers from arthritis could be saved for a useful life by the methods of treatment now at our command.

Schauffler,<sup>24</sup> writing on the subject of chronic arthritis, urged that every physician use some simple method of classification and familiarize himself with the major characteristics of each group in order that he might treat his patients to the best advantage. He has found the most serviceable clinical grouping to be that of Goldthwait: (1) infections; (2) atrophic; (3) hypertrophic arthritis. He stated his belief that the pure infectious type is always due to bacterial infection. The atrophic type is of a different character. The patients are usually of the viscerotropic type and have always been somewhat delicate. There is usually a history of worry, overwork or mental shock, and there is evidence of disturbed body chemistry or of endocrine imbalance.

24. Schauffler, Robert M.: Arthritis, *J. A. M. A.* 89:1748 (Nov. 19) 1927.

only from 2 to 3 per cent. In a series of 107 cases, the distribution according to sex was males, 97; females, 10. Thomas believed that the precipitating factor is not infrequently trauma, either directly to the joint or indirectly in the form of ill advised or careless urethral instrumentation and treatment, excessive activity or sexual excitement during the acute stage of the urethritis. The arthritic symptoms usually manifest themselves during the second or third week; the earliest case recorded is five days. However, involvement of the joints may supervene at any time throughout the acute or chronic course of the disease or in the presence of urethral or uterine adnexal complications. In Thomas' experience, the symptoms have been polyarticular in 58 per cent and monarticular in 42 per cent. The joints have been involved in the following order of frequency: knee, 58 cases; hip, 50; wrist, 21; shoulder, 19; phalangeal, 17; elbow, 13; metatarsophalangeal, 8; spine, 8; metacarpophalangeal, 7; sacro-iliac, 1; temporomaxillary, 1, and sternoclavicular, 1. In respect to treatment, Thomas called attention to what he believes is a current mistake on the part of the orthopedic surgeon and the genito-urinary surgeon; namely, that they center too much on the treatment of the joint or the prostate or the seminal vesicles as the foci of infection, with apparent lack of appreciation of the fact that the condition is a septicemia. Thomas felt that the first step should be to treat the blood stream infection either by biologic therapy or by chemotherapy; second, to eradicate the focus or foci of infection in the genito-urinary tract, and third, to treat the involved joint or joints by local methods.

*(To be Continued)*

Smith<sup>28</sup> expressed the belief that intestinal stasis is responsible for many cases of polyarthritis, and that in certain cases surgical intervention to relieve the cause of it is required. However, this should never involve resection or sidetracking of the involved portion of the intestine. He also believed that implantation of *Bacillus acidophilus* in the cecum is helpful in certain cases.

[ED. NOTE.—Surgeons were at one time enthusiastic in the attempt to relieve persons with intestinal stasis by operations. Numerous operations were performed in different disease conditions, including arthritis. The results were disappointing, and the radical method of treatment has been generally abandoned. Smith obtained some interesting results, and his work is suggestive and should be continued. Its chief value at present, however, is again to call attention to the importance of the intestinal factor in the treatment of persons with arthritis. The present armamentarium of the physician is varied and large enough to deal with this condition without resorting to operation.]

*Treatment of Arthritis with O-Iodoxybenzoic Acid.*—Of twenty-one patients with chronic arthritis who were treated with salts of o-iodoxybenzoic acid, Cottrell<sup>29</sup> found that all but three showed improvement. The relief of pain was often prompt and marked. In the majority of chronic cases, there was an improvement of function from a slight to a marked degree. In the author's opinion the drug is best given in courses of from six to eight doses semiweekly, with from three to six weeks' rest between each course. Intravenous administration is the method of choice, although the drug may be given orally in capsule form. The latter may be followed by nausea.

*Gout.*—According to Harbinson,<sup>30</sup> gout is probably often overlooked. All parts of the body should be examined for tophi. It should be remembered that in this condition bursae often become inflamed. The diagnosis is made by examination of the tophi. The author places considerable reliance on the determination of blood uric acid and advises that this examination be made in every patient with obscure pains in the joints. A blood uric acid content of more than 5 mg. is suggestive of gout. Other conditions in which the blood uric acid may be high are leukemia, polycythemia, interstitial nephritis and febrile states. The treatment is dietary, with purines eliminated. The protein may be high. Quinidium is still the best drug to use.

*Gonorrheal Arthritis.*—Thomas<sup>31</sup> wrote that the incidence of arthritis as a mercurial complication of gonorrhea is not great, averaging

28. Smith, Res.: J. Bone & Joint Surg. 16:57 (Jan.), 1934.

29. Cottrell, J. E.: Am. J. M. Sc. 174:523 (Nov.), 1927.

30. Harbinson, J. E.: California & West. Med. 27:332 (Sept.), 1927.

31. Thomas, E. A.: Gonorrheal Arthritis, J. A. M. A. 89:3174 (Dec. 24), 1927.



at that time, which is composed only of the identical tissues that are in state of active hyperplasia in the normal parts of the same breast.

(a) *At Birth and Puberty.*—My conclusions are based on examinations of the breasts of children (male and female) who were born dead; of those who were in the years immediately preceding puberty and of those who were at the age of puberty. The deaths of many of the children whose breasts were examined occurred at full time and were due to traumatic causes; the conditions of their breasts could not possibly

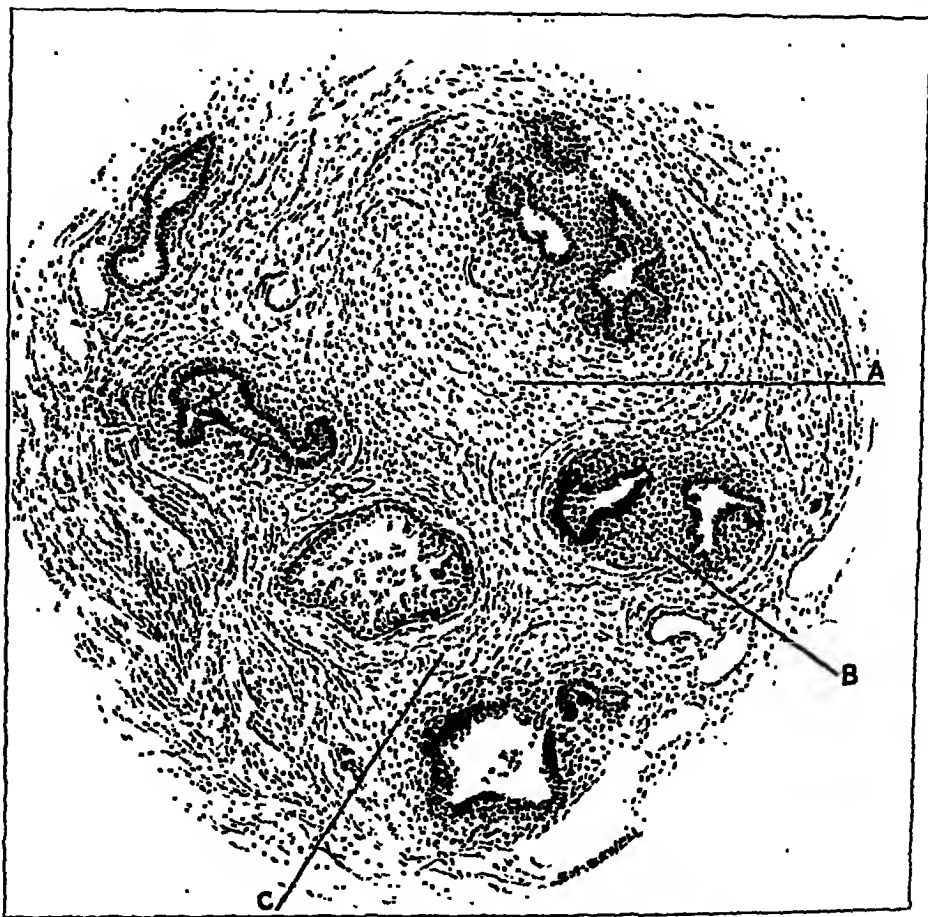


Fig. 1.—Microscopic appearance of part of a male breast at birth—full term. The death was caused by a rupture of the tentorium during birth. At A, B and C, the pericanalicular and periacinous connective tissue is in a state of hyperplasia among the fibers of which lymphocytes have accumulated. There is a desquamative epithelial hyperplasia in the acini and terminal ducts. There is no elastica in this breast. Compare with figure 2.

be assigned to antenatal disease. The morphologic appearances I describe are those of normal active changes and are present in varying degrees in all breasts at birth and at puberty.

It is impossible to distinguish between male and female breasts at birth, but the subsequent changes, at puberty, for example, are more marked in females; therefore, I shall describe only female breasts in

## "CHRONIC MASTITIS," "CYSTO-ADENOMA" AND ADENOMA OF THE BREAST

G. LENTHAL CHEATLE, F.R.C.S.

LONDON, ENGLAND

In writing this paper, I have had several objects in view. The first object is to place the so-called "chronic mastitis" in its correct etiologic and pathologic position. Its morphologic appearances are identical with those of the physiologic active state at birth, at puberty and in certain phases of lactation (fig. 1). This active state becomes pathologic (fig. 2) when it is present at from about 30 to 45 years of age and induces diffuse pain, and when fibro-adenomas (usually of the same type as those which form at puberty) develop in its occupied areas (figs. 3 and 4). These two separate occurrences belong to the condition to which the term "chronic mastitis" is so universally applied.

A second object is to point out that the commonest type (fig. 6) of fibro-adenoma that occurs at puberty is a local exaggeration of the physiologic and active hyperplasias which are normal at puberty. A third object is to point out the importance of a state-of formations of epithelial tumors in the ducts and acini—which crops up in the literature. of a pathologic condition in several guises and disguises, including that of "cysto-adenoma." A fourth object is to describe a true adenoma of the breast.

### ETIOLOGY AND PATHOLOGY OF CHRONIC MASTITIS

In this part of my paper I shall describe (a) the similarity between the normal active morphologic appearances present in the breasts at birth, at puberty and in lactation;<sup>1</sup> (b) the etiologic connection between the activity of the breasts at birth, at puberty and in certain phases of lactation, and the morphologic appearances which are now commonly associated with the term chronic mastitis, and (c) the etiologic association that exists between the general active changes of the breast at puberty and the formation of the commonest type of fibro-adenoma that arises.

1. While writing the results of my investigations, my attention was called to some of the contents of an article by John Fraser (Surg. Gynec. Obst. 45:200 [Sept.] 1927). I am glad to see that he shares my conviction that the best method of examining breasts is to cut whole sections of the glands—a practice which I have adopted and taught for thirty years. I cut the whole sections in paraffin, not in celloidin.

these periods. The changes occur mainly in the terminal ducts and acini, and concern hyperplasia of the epithelial, pericanalicular and periacinous connective tissue.

At birth, the epithelial hyperplasia may be one of two kinds, one type being desquamative and the other formative or genetic. That one type may sometimes be more obvious than the other depends on the stage reached in development. The desquamative type belongs to the



Fig. 4.—Microscopic appearance of the fibro-adenoma *B* in figure 3.

later stage. I will not refer to the formative type here; I may say, however, that these genetic morphologic appearances are like the more dangerous states of dysgenetic epithelium which are seen in pathologic glands in later life.

In the desquamative type of epithelial hyperplasia at birth, to which I now refer, the ducts and acini of the whole breast are filled by small, irregularly shaped, badly staining epithelial cells which have been cast off and are incapable of further life. Also, around the ducts and acini of the whole breast there is an extensive hyperplasia of rather loosely constructed pericanalicular and periacinous connective tissue among the



Fig. 2.—Photomicrograph of part of a whole section of breast removed from a married woman, aged 38, who had three children, the youngest being 8 years old. Extreme pain in this breast had been borne for eight or ten years. The photograph has been taken at the posterior margin of the breast *D*. At *D* there is a slight undulation which would not be appreciated by digital palpation. *B* points to a lobule in which there is hyperplasia of the pericanalicular and periacinous connective tissue among the fibers of which lymphocytes have accumulated. In the terminal duct *A* there is a desquamative epithelial hyperplasia (type a) which can be seen in the acini. The epithelial hyperplasia is distending these structures. There was no discharge from the nipple. Compare with figure 1.

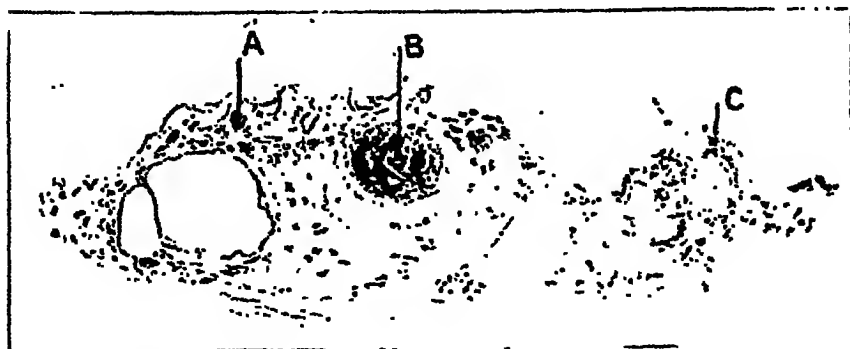


Fig. 3.—Microscopic appearance of section of whole breast which was removed subcutaneously from a married woman, aged 42. Multiple cysts and pain were the cause of its removal. In the more dense looking parts of the section, there were the same signs as those seen in figures 1 and 2. In addition, at *A*, *B* and *C* there were fibro-adenomas in various stages of formation, of which *B* is the most advanced. They belong to the type of the usual fibro-adenoma which occurs at puberty.

complain of diffuse pain in their breasts. The morphologic appearances in these breasts are those on which the supposed manifestations of inflammation are based. They cannot be regarded as being inflammatory any more than can the same active normal signs which are present at birth and puberty.

Paradoxical as it may seem, "chronic mastitis" is really a physiologic process which has become pathologic by being present when it should be absent, by developing an excess of desquamative epithelial hyperplasia which induces pain by distention (fig. 2 *A*) and by possessing the same liability as the breast at puberty to form fibro-adenomas which may or may not develop acini within their formations of tumor (figs. 3

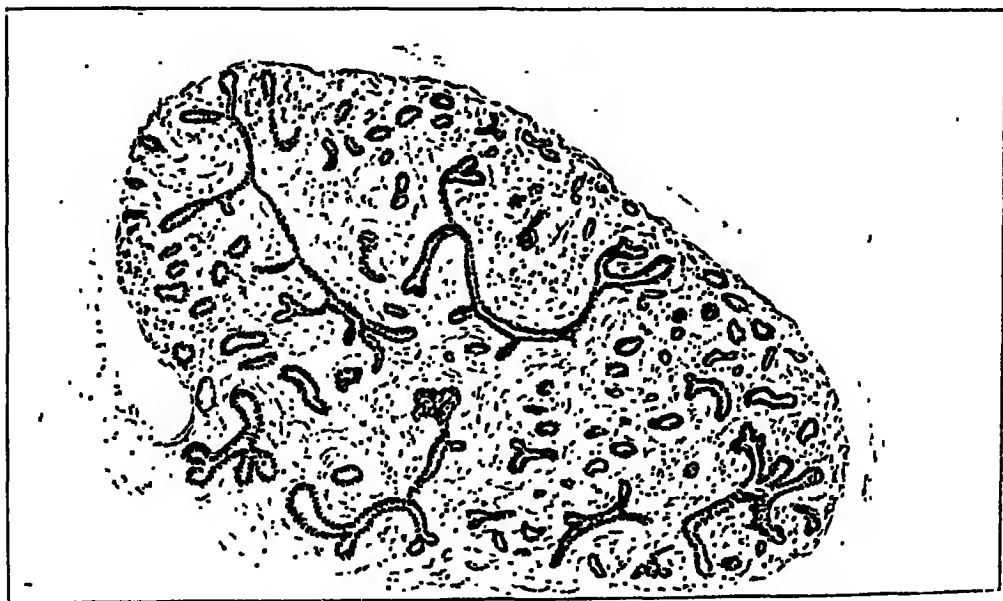


Fig. 6.—Microscopic appearance of a small fibro-adenoma taken from *B* in figure 5. It is the usual type of fibro-adenoma that occurs at puberty and shows the dense hyperplasia of the periacinous and pericanalicular connective tissue.

and 4). For some inexplicable reason, the breasts of some women at any age between 30 and 45 exhibit the state seen at birth and at puberty.

A new and more descriptive name than chronic mastitis is wanted; in my previous communications on the subject I have described it under the heading of "Desquamative Epithelial Hyperplasia type A." I do not look on it as a dangerous state, and it may remain uncomplicated by another pathologic process.

Clinicians are apt to describe these breasts as being nodular all over their anterior surfaces. The posterior surfaces, which are clinically inaccessible, are smooth (fig. 2 *D*). The anterior surfaces of these breasts, and of most breasts of women at this period of life, are presumed to be nodular, for the following reason: As the glands become

fibers of which lymphocytes are present (fig. 1). These appearances are constant, and I regard them as part of a normal physiologic process of development.

This enormous activity ceases in the years between birth and puberty and after lactation. After birth and before puberty, the desquamative epithelial hyperplasia ceases; there is often almost a complete atrophy of the pericanalicular and periacinous tissue, and the connective tissue that is more obvious than any other is the ordinary supporting connective tissue of the breast.

At puberty the whole condition seen at birth recurs in more regular and less rampant formation, and lymphocytes also reappear among the increased and actively reforming pericanalicular and periacinous con-

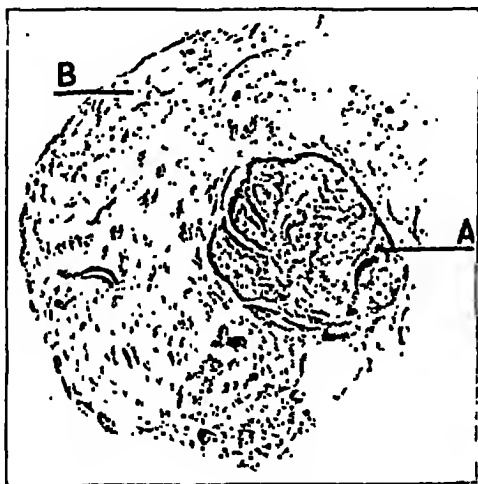
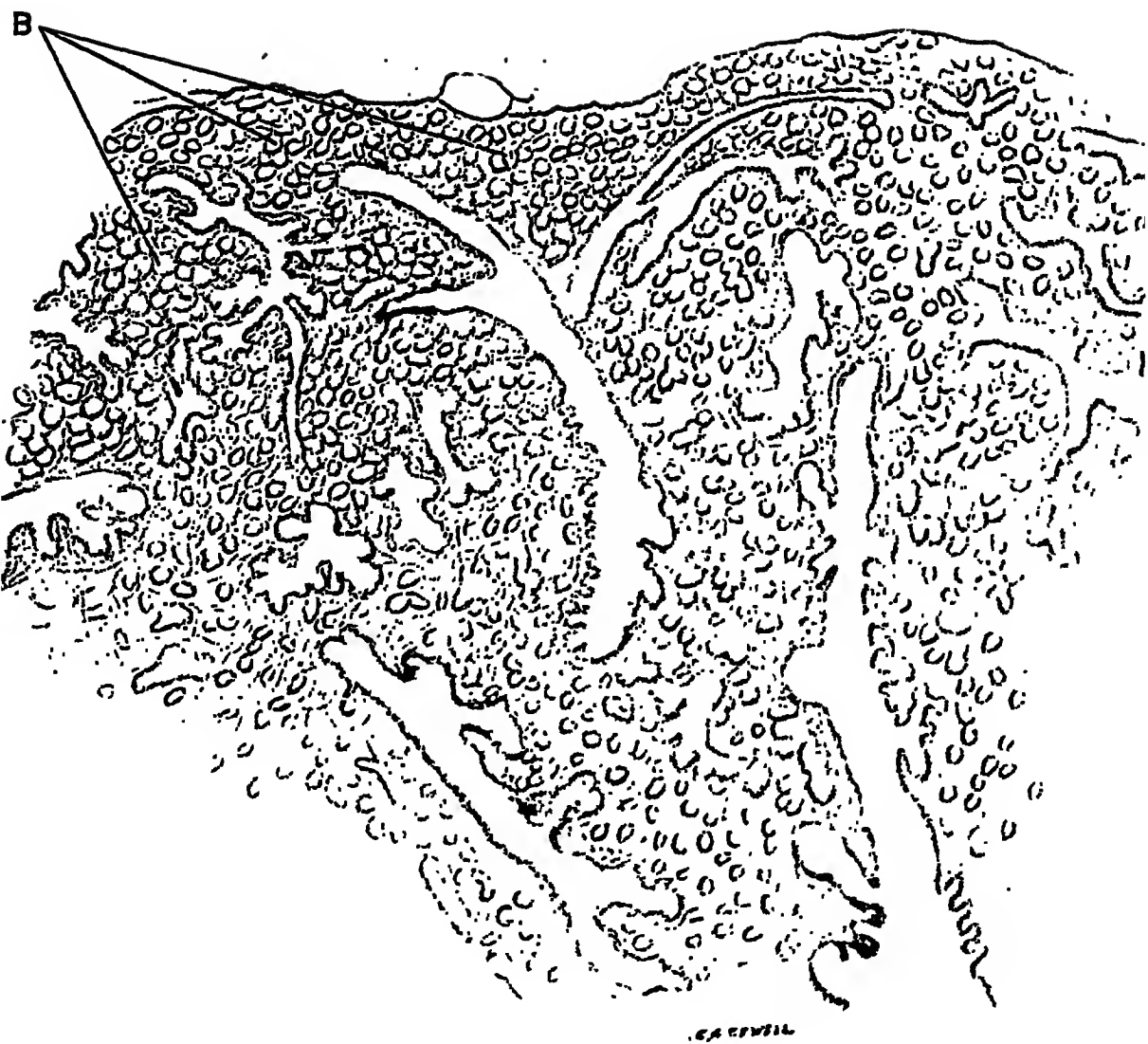


Fig. 5.—Microscopic appearance of a segment of breast removed from a married woman, aged 22, who had noticed the lump *A* for four years. *A* is a fibro-adenoma belonging to the type that usually occurs at puberty. Figure 6 shows *B* in this figure. On the edge of the tumor at *A* there has been an enormous increase of normal looking acini (see fig. 7 *B*).

nective tissue. New acini form and take their part in the enlargement of the breast. After puberty, there is again a great deal of atrophy of the acini and also of the pericanalicular and periacinous connective tissue and a cessation of desquamative epithelial hyperplasia. The appearances of this latent state may remain more or less constant throughout life if lactation does not occur. I now pass on to the merging of these normal changes into pathologic states.

(*b*) *Etiologic and Morphologic Appearances.*—In the first pathologic state, namely, the so-called "chronic mastitis," the morphologic appearances in the epithelium and pericanalicular and periacinous connective tissues are identical with the active states I have described in breasts at birth and at puberty (compare fig. 2 with fig. 1). They are seen between the ages of 30 and 45 in many women and in a few men who





A

Fig. 7.—Microscopic appearance of section taken from the edge of the tumor in figure 5. At *B* there is an enormous increase in the number of acini which do not differ in appearance from those in the rest of the section. The duct has been stained, and it has undergone a slight irregular hyperplasia around the ducts of the tumor.



former, instead of being comparatively loose, is much more dense and compact than in the rest of the breast and affects only a segment of the breast. The size of the segment affected differs in various tumors. The epithelial changes are also those of desquamative epithelial hyperplasia. In some of these tumors of puberty there is also an enormous

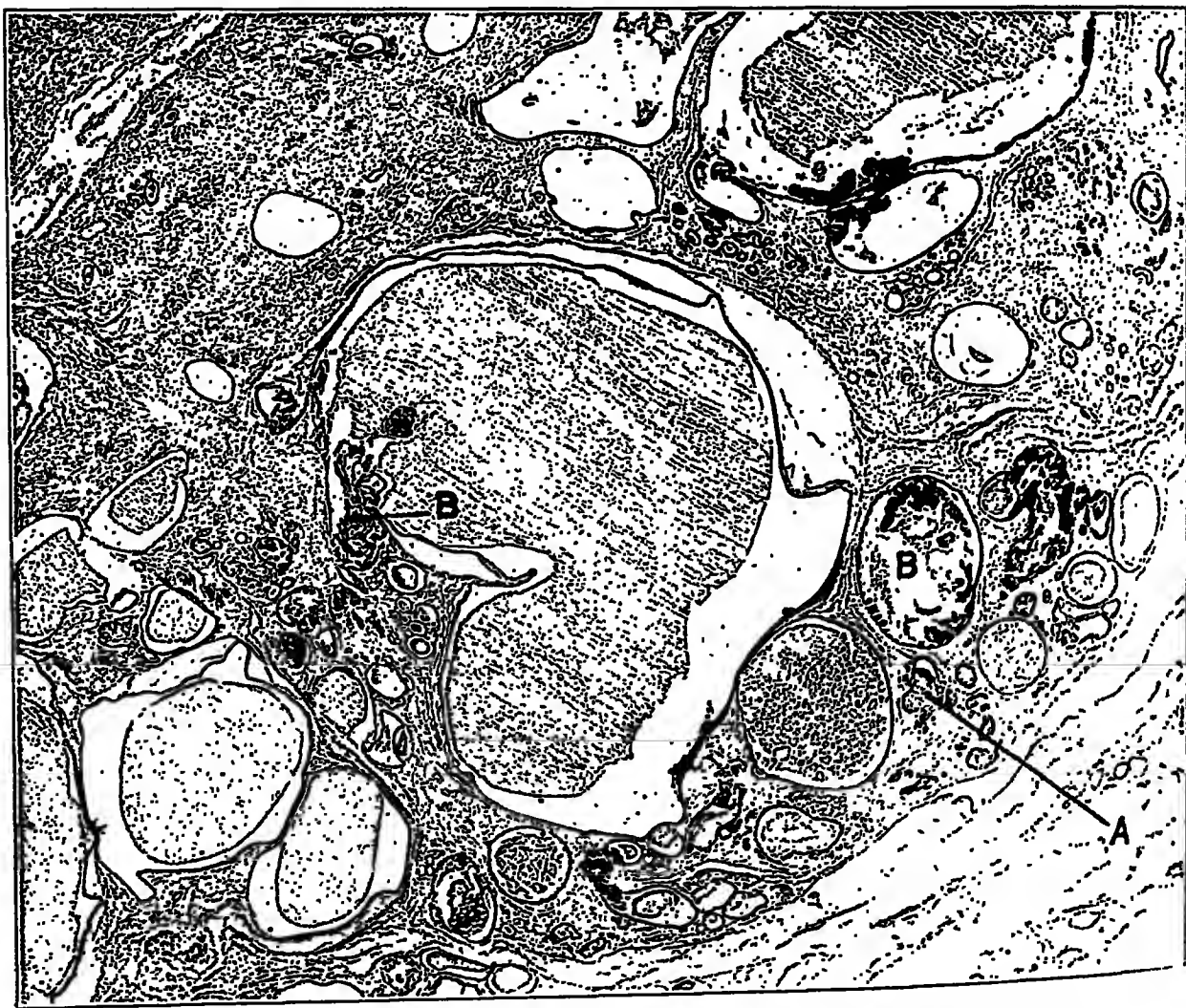


Fig. 9.—Photomicrograph taken from figure 8. *B* and *B* is a dilated duct containing papillomatous and sessile dysgenetic epithelial hyperplasia. At *A* there is a collection of acini which are distended by the same type of sessile epithelial growth.

development of acini (fig. 7) which further accentuates a perverted likeness to the physiologic hyperplasia that is occurring in the rest of the breast at puberty. I particularly wish to point out that this tumor commonly begins at puberty and originates in the same tissues that are normally active at puberty. The whole tumor may be regarded as being a more or less localized perversion of a normal physiologic state.

pendulous, and especially after lactation, the ligamenta suspensoria of Sir Astley Cooper become thickened. The thickened branches as they approach the skin to which they are attached include fat lobules which are so isolated in the process that they appear as separate nodules. If the skin of these breasts is undercut the cutaneous attachments of these ligaments are divided, and the underlying structures then feel smooth, and nodularity is not found.

(c) *Etiologic Association Between Active Changes in Breast and Fibro-Adenoma.*—The second pathologic condition to which I refer is the etiologic connection that exists between the active (figs. 5, 6 and 7)

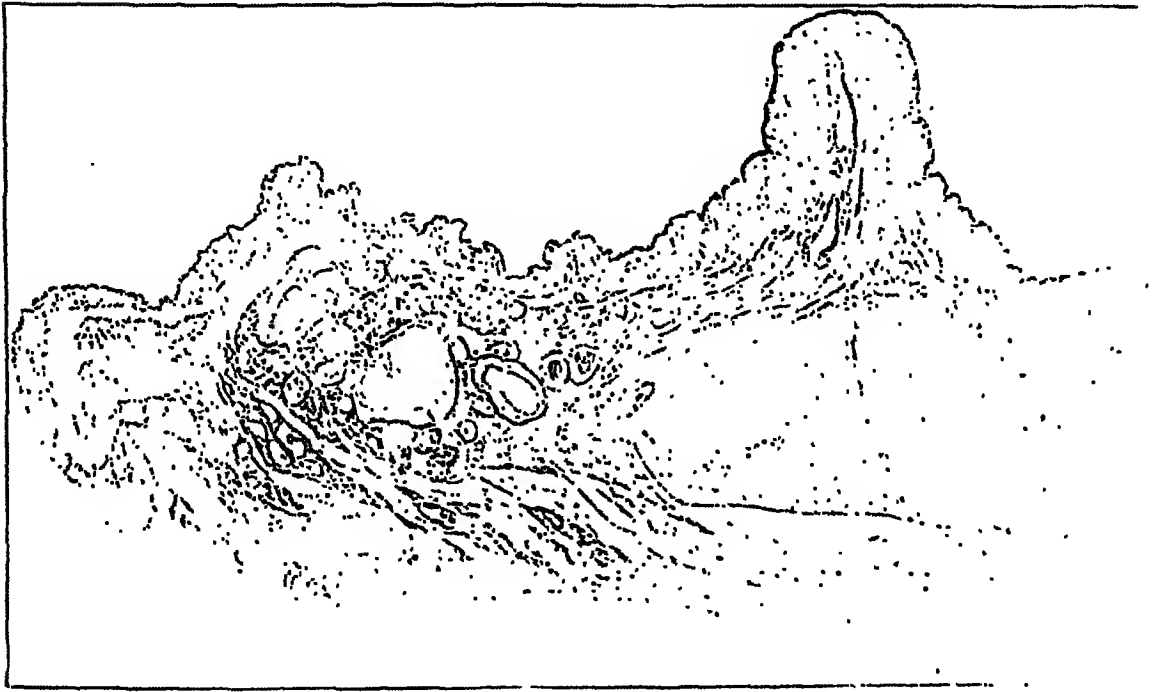


Fig. 8.—Photomicrograph of whole horizontal section of breast from a married woman, aged 36. Removed for the presence of the localized painful nodularity due to the lesion seen on the left of the section. The affected duct and its branches can be seen to be dilated from the prominent nipple in the center of the section to the periphery where there are comparatively large cysts which contain dysplastic epithelial hyperplasia seen at A and B of figure 9 and at A and B of figure 10. Carcinoma is not present in this breast. There was no discharge of any kind from the nipple.

changes at puberty and the formation of that type of fibro-adenoma which is the most common one at that time. Precisely the same tissues which form this tumor are actively undergoing normal hyperplasia in other parts of the breast at the same time; the pathologic difference between the fibro-adenoma and the rest of the breast is that the hyperplasia of the pericanalicular and periacinous connective tissue in the

must be negligible when compared with the new glandular formation that occurs in the adenoma described in the latter part of the paper; (2) that it is commonly composed of a series of separate tumors—papillomas and sessile epithelial growths in preexisting ducts and acini—

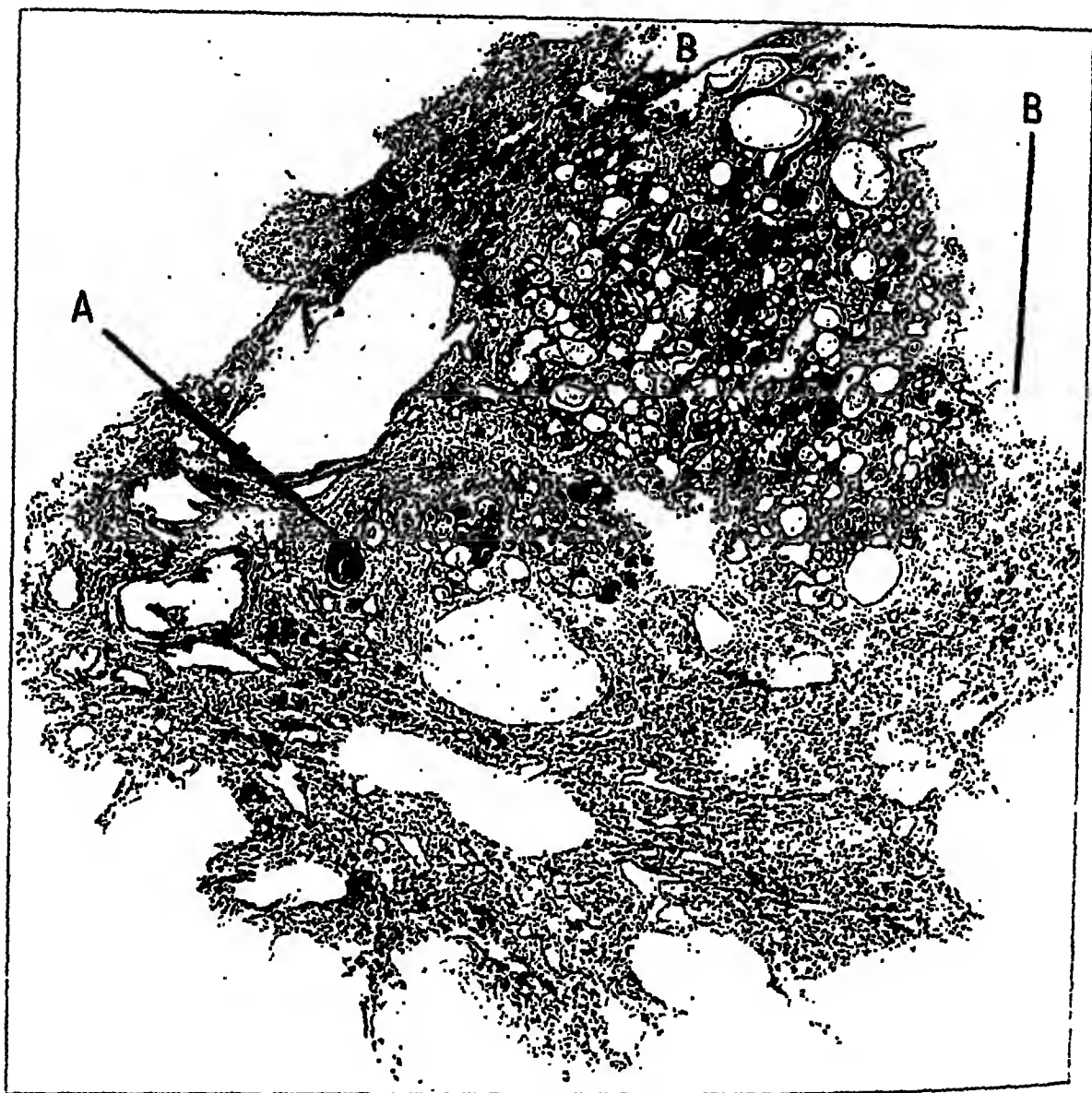


Fig. 11.—Photomicrograph of whole section of breast in which are all the morphologic appearances seen in figures 8, 9 and 10. The section was made vertically in order to show the triangular form of the state described in the text. *A* points to the apex of the triangle in front of which the nipple was situated. The lines *BB* point to the limits of the base of the triangle. The lesion was in the depths of the breast. Palpation revealed only a density in its area of occupation. Carcinoma is not present in this breast. There was no discharge of any kind from the nipple.

Recognition of the fact that there is an etiologic connection between the pathologic changes I have mentioned and physiologic activity makes a clear and comprehensible point from which to begin consideration of all problems related to the incidence and genesis of pathologic (dys-genetic) hyperplasia.

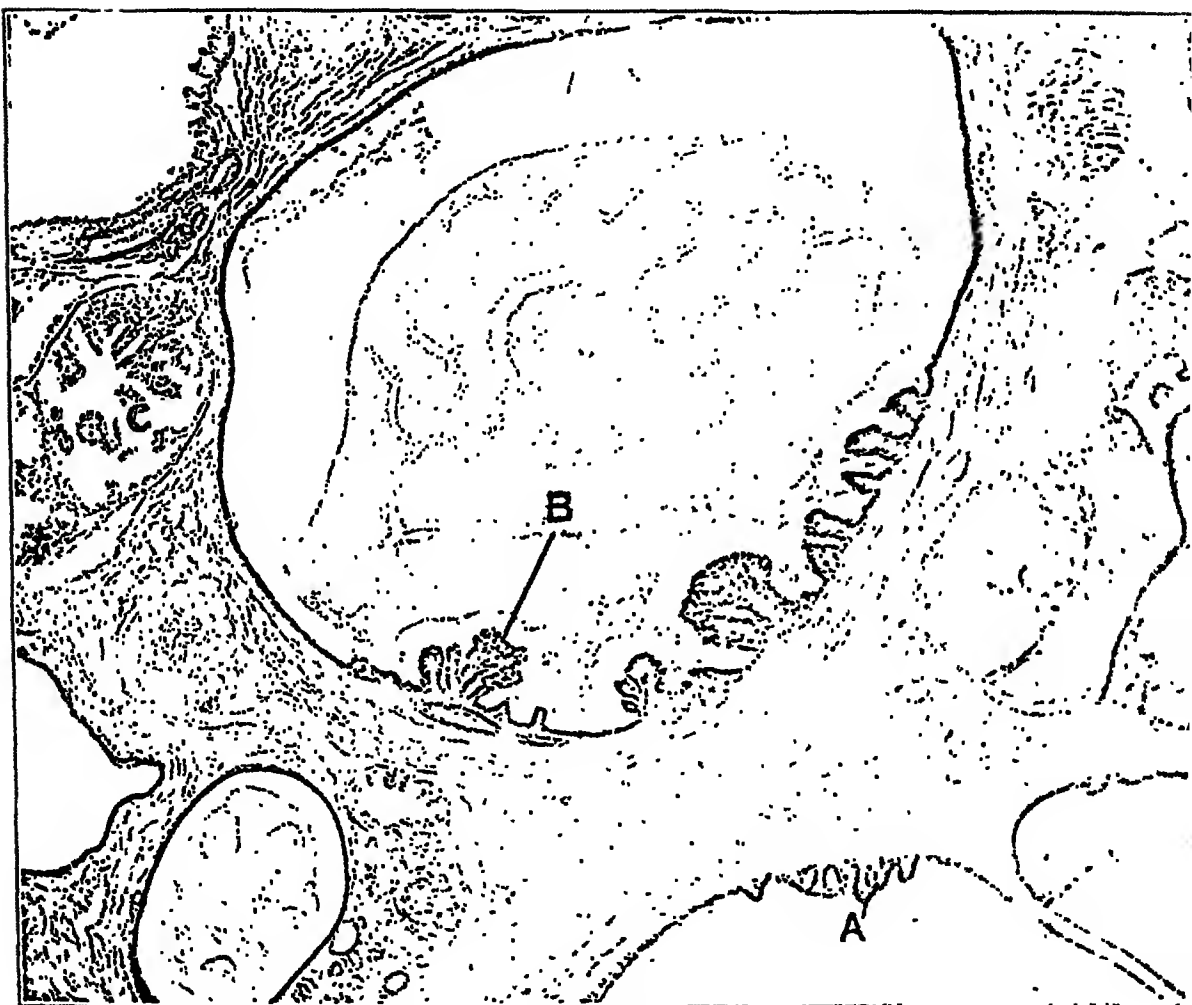


Fig. 10.—Photomicrograph taken from figure 8. In the dilated duct (A) small isolated origins of multiradicular papillomas can be seen. The epithelial layer covering the tips of some of the stalks has already joined with that covering the tips of stalks in juxtaposition to each other. Alveolar spaces lined with epithelium are formed in this way. In the dilated acini (C) the epithelial hyperplasia is passing from the desquamative to the dys-genetic type.

#### DESCRIPTION OF CYSTO-ADENOMA

My object in this part of the paper is to describe the tumor now termed "cysto-adenoma" and to point out that it is not to be considered that there is any new formation of acini, and that it is not

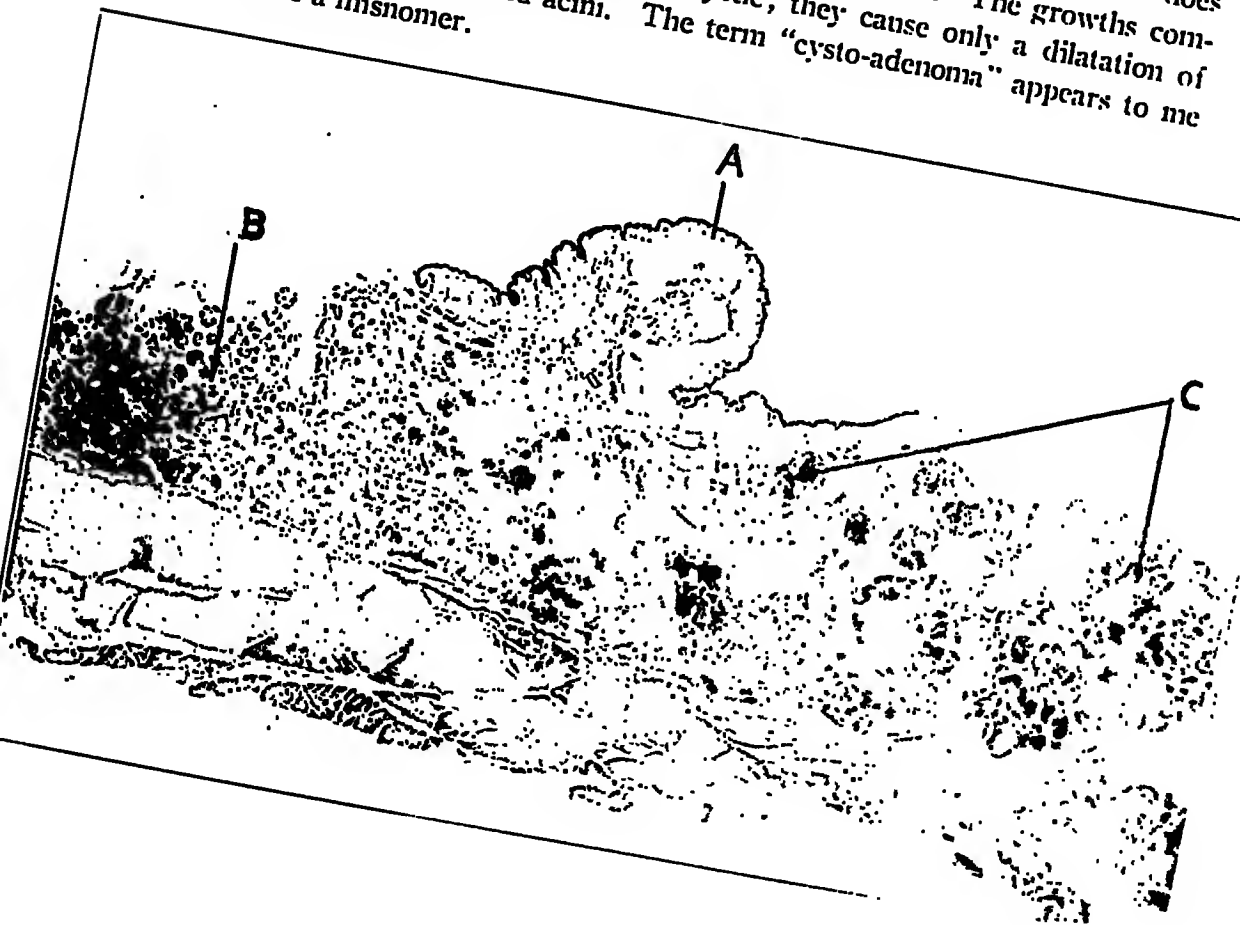
cysto-adenoma of the breast has no more right to the term than the multiple adenomatous papillomas of the colon, which the changes in cysto-adenoma of the breast so closely resemble. No one suggests calling the condition in the colon cysto-adenoma. The origin of the term as applied to the breast can be explained in the following way: The ducts of the breast are not of large caliber like the tube of the



Fig. 13.—Photomicrograph taken from upper and central parts of the lesion *C* in figure 12. The ducts are full mainly of papillomas, and the dilated acini are distended by a sessile epithelial hyperplasia. They are more obvious around the margins of this section. *A* marks the spot in which the carcinoma had begun (see fig. 14).

colon; they are tubes of small caliber which become convoluted and distended and when cut in sections for microscopic examination look like separate cysts, whereas they really are parts of convoluted tubes in perfect continuity. It is important to know all about this state, because it

and greatly resembles the condition of multiple adenomatous papillomas in the large intestine.<sup>2</sup> In the breast, the epithelial hyperplasia may be more sessile than papillomatous and vice versa; (3) that it is usually a much more diffuse condition than it is generally supposed to be; (4) that it is as full of danger to the patient as the multiple adenomatous papillomas of the colon, and (5) that the term "cysto-adenoma" does not convey correctly the actual state of the tumor. The growths composing the state do not become cystic; they cause only a dilatation of preexisting ducts and acini. The term "cysto-adenoma" appears to me to be a misnomer.





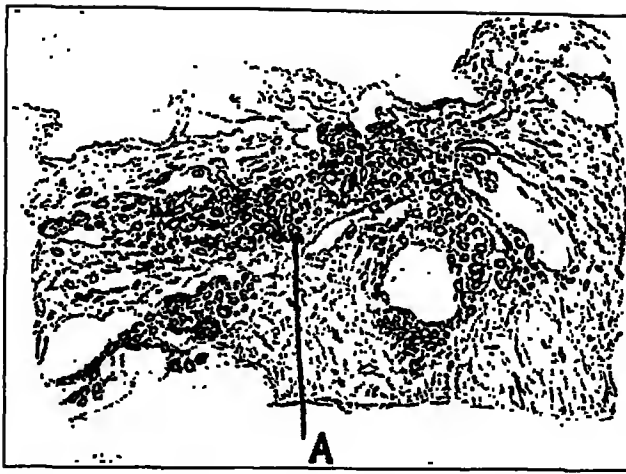


Fig. 15.—Part of a whole section of a breast removed from a married woman, aged 44. Removed for pain which corresponded in situation to an area of density. There was no discharge of any kind from the nipple. The epithelial hyperplasia was papillomatous in the ducts to a much less degree than in the breasts shown in figures 8, 11 and 12, and was much more sessile in character. There is early carcinoma in this breast at *A*, shown in figure 16. The axillary lymphatic glands were not affected.

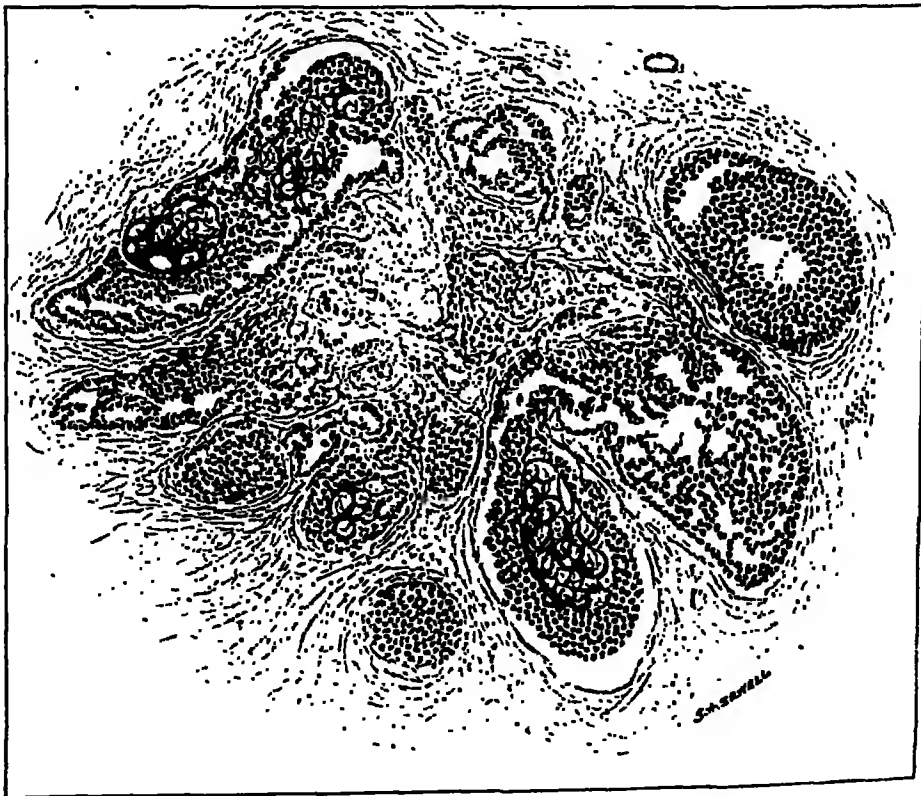


Fig. 16.—Drawing of *A* in figure 15 under higher magnification showing terminal ducts and acini filled with a sessile dysgenetic epithelial hyperplasia. In two of the terminal ducts, it has undergone colloid degeneration. Some epithelial cells have escaped and are invading the connective tissue of the breast.

is often regarded rather casually as being free from danger, whereas, in reality, it is so pregnant with probable danger in all instances and with positive danger in some that when it appears most benign it should be regarded as closely allied to carcinoma as the multiple adenomatous papillomas of the colon. On the other hand it is sometimes described, in exaggerated examples, as being carcinoma, when in reality all the





is not present in these breasts. In figures 12, 13, 14, 15, 16 and 17, the distribution of the disease is affecting precisely the same regions. In figure 16, taken from figure 15, and in figure 14, taken from figure 12, there is undoubted carcinoma which has spread among the supporting connective tissue of the breasts and has not affected the fat outside the breast nor the axillary lymphatic glands. The same state may be seen in the ducts and acini of figure 17. In this specimen the carcinoma has invaded the connective tissue of the breast, has undergone colloid degeneration and has spread to one lymphatic gland in the axilla.

When carcinoma does not originate purely in the terminal ducts but when its acini also contain the original malignant epithelial hyperplasia, the state can be seen without exception in every early case of carcinoma of the breast, and sometimes it can be demonstrated—if the elastica is particularly stained—in late cases of carcinoma when nearly

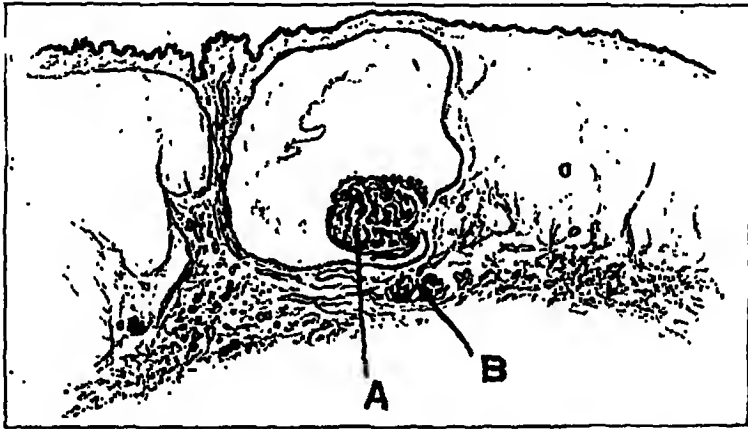


Fig. 18.—Drawing of a whole section made from the breast of a married woman, aged 56. There is a large dilated duct, on the right of the nipple, in which there is a tumor (*A*) with a papillomatous attachment to its wall. The continuation of the duct is also dilated and contains papillomatous and sessile epithelial hyperplasia (*B*). There was no discharge of any kind from the nipple. The tumors were benign.

all the morphologic evidence of its site of origin has been lost in the chaos of growth and spread. Lastly, it is an important and dangerous state on account of its clinical obscurity when it exists in the substance of the breast, both when carcinoma has not begun and also when carcinoma is present in its earliest stages. If the condition appears in a duct the distribution of which is on the surface of the gland, and when there is only a thin layer of fat between it and the skin, as shown in figures 8 and 12, its presence can be detected by a localized triangular nodularity with the base toward the periphery of the gland (figs. 11 and 17). I cannot exaggerate the importance of local nodularity as a clinical sign. When it affects a surface diet and when the layer of fat

the complete distribution of the epithelial growth can be seen to be diffuse in the affected ducts much more often than is generally supposed. With the aid of these large sections and also with that of certain clinical features, I will next point out the importance and danger of the subject. Later, I will describe the nature of the epithelial hyperplasia.



as it traverses the gland to reach the periphery and a short branch directed backward to reach the posterior surface of the gland. Throughout the courses of ducts, lobules of acini are connected to them by smaller ducts. During lactation, the nipple is crammed with acini and is distended to so great an extent that morphologically they appear to be the main constituents of the nipple. After lactation, they disappear completely.



Fig. 20.—Tumors *B* situated lower down in the same duct *A* of figure 18. The papillomas have undergone the same development into glandular reproductions of less typical character compared with *A* in figures 18 and 19.

The epithelial hyperplasia of this so-called "cysto-adenoma" may exist only in the duct as it passes through the nipple or only in the ampulla of a duct, or it may exist only in the main branch before it divides (figs. 18 and 21). On the other hand, it may extend throughout the whole course of a duct from the ampulla to its periphery and involve the acini to such an extent that they all contain some form of

between it and the skin is thick, its clinical signs on palpation resemble the same condition when it is in the substance of the gland. In both these instances it appears as a localized lesion, harder than the rest of the gland and incapable of further diagnosis by palpation. Pain that usually accompanies this state is always referred to this denser area of the breast. There may also be a history of an intermittent discharge of



ous even than the purely papillomatous type. In the ducts the epithelial hyperplasia behaves a little differently from that in the acini. It may affect the duct in two ways. First, it may be papillomatous. When the tumor is of this type it arises in a multiradicular manner from many stalks of fibrous tissue which are usually composed of the whole wall of the duct, and the elastica can be stained in their centers (figs. 10 *A* and *B*); or, less commonly, it may arise from the intra-elastica connective tissue, when there is no elastica in the stalks. However papillomas arise, they are always covered by the columnar epithelium of the duct. The papillomas arising from the intra-elastica do not branch so freely as those which contain the elastica; they remain small, and epithelium piles itself on the top of them. The papillomas containing the

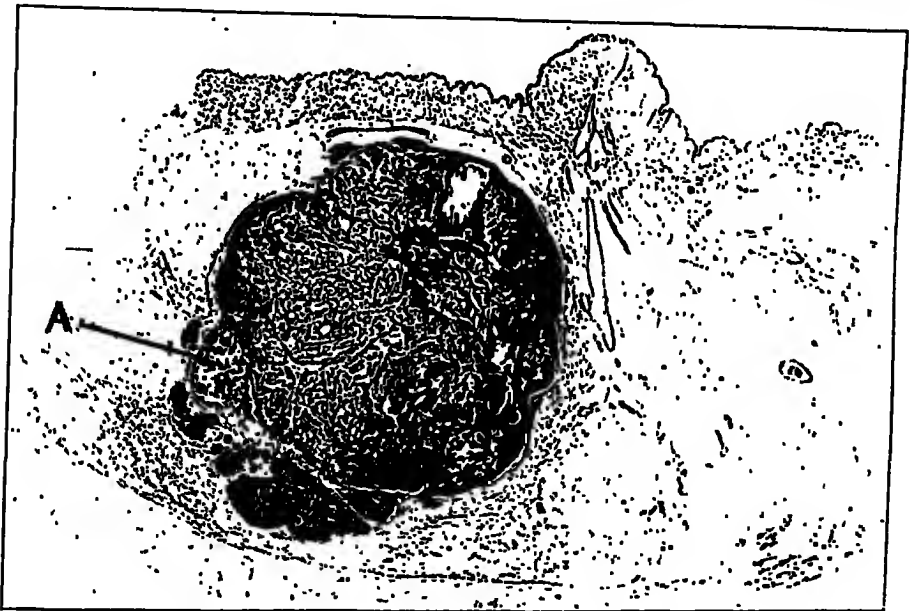


Fig. 22.—Photomicrograph of whole section of breast removed from a married woman, aged 48. The main part of the epithelial hyperplasia is confined within the boundaries of normal ducts and has a decided papillomatous arrangement of less orderly character than that in figures 18, 19, 20 and 21. At the lower left part of the periphery of the tumor, epithelial cells have invaded the connective tissue. There was no discharge of any kind from the nipple, and the axillary lymphatic glands were not affected.

elastica may undergo various changes. They may appear as small growths, but usually they branch extensively and the epithelium on the tips of their branches coalesces with branches of the parent papilloma and with those of contiguous stalks to form alveoli lined by epithelium (figs. 10 *A* and *B*). A papilloma may more rarely develop into an arrangement which constitutes a small mammary gland or adenoma containing ducts and acini (figs. 18 and 21). When this process occurs,

the dysgenetic epithelial hyperplasia. I have a specimen—presented to me for examination by Mr. Sampson Handley—in which the whole lengths of two ducts and their acini are involved in this manner. Again, only one of the main branches may be thus affected throughout its course (figs. 8, 11, 12, 13, 15 and 17) or even a few or only one of its terminal branches and acini may contain the epithelial hyperplasia. There are no clinical signs on which a limited distribution can be diagnosed from an extensive one, and no one can tell from clinical signs whether he is dealing with a growth only in the ampulla or



tain a carcinoma; for example, it is hard to believe that all the epithelial changes seen in *A*, in figures 22 and 23, in which carcinoma is present, did not begin in this way, and it is probable that the advanced carcinoma in figure 24 is an advanced tumor which had the same origin. Accompanying the papillomatous tumors there is generally a sessile epithelial hyperplasia without any fibrous stalks, which may completely fill a portion of a duct. Sessile and papillomatous formations are commonly seen together when long branches of ducts are affected. Sometimes the sessile epithelial hyperplasia is more in evidence than the papillomatous. If that is so, the state is more dangerous than if it were chiefly papil-

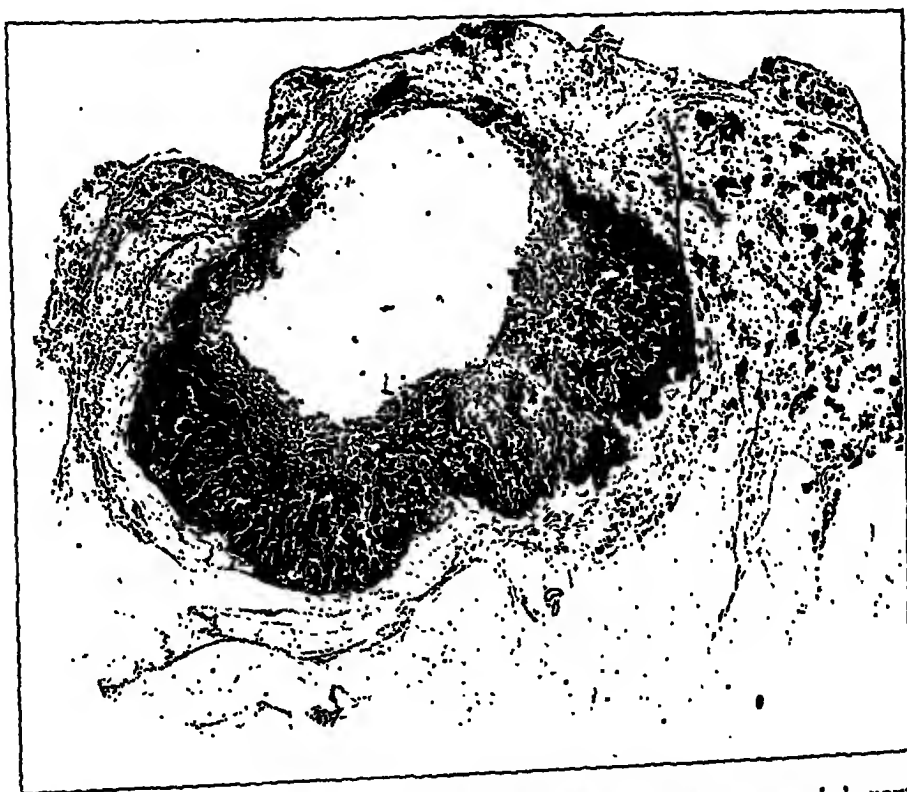


Fig. 24.—Photomicrograph of whole breast removed from a married woman, aged 36. There was no discharge of blood from the nipple. Lymphatic glands in the axilla contained carcinoma. The patient died of the disease eight months after the radical operation. The extension of this carcinoma was one of the most rapid and diffuse the author has seen. The appearances suggested a papillomatous arrangement, and the epithelial cells were columnar. The three tumors depicted in figures 18, 19, 20 and 21 appear to be benign examples of a state which may pass on to the malignant condition seen in figures 22, 23 and 24.

lomatous. For instance, when only a terminal duct and its acini are affected, the epithelial hyperplasia may be only sessile in the ducts and acini. The acinous papillomas are not so common, and when they occur they are composed of fine fibrillous stalks which do not branch

it usually takes place in the main duct. It is interesting to observe that all the epithelial and glandular elements of this particular intracanalicular tumor (figs. 19 and 20) are derived from the columnar cells which originally lined the duct.





distended boundaries. The changes may exist in a breast in which carcinoma is not present. There are examples in which at some place or other the epithelial cells have invaded outside structures and unsuspected carcinoma is present (figs. 2, 13, 14, 15 and 16). It is difficult to discover the focus of exit of these invading cells, even after examination of sections carefully cut in series.

#### PURE ADENOMA OF THE BREAST

My object in this part of the paper is to describe the purest type of adenoma I have observed in the breast. It is a rare and benign



Fig. 26.—A representative part of the adenoma *A* in figure 25.

tumor. On the one hand, it differs from the cysto-adenoma by a massive new formation of pathologic adenomatous elements—a new formation of ducts and acini does not occur in cysto-adenoma. On the other hand, the pure adenoma differs from a fibro-adenoma, in which a new formation of ducts and acini may occur (fig. 7), by a complete absence of the dense hyperplasia of the pericanalicular and periacinous connective tissue which is characteristic of fibro-adenoma (fig. 6). The pure adenoma resembles the cysto-adenoma by exhibiting papillomatous and sessile epithelial hyperplasia which dilates the structures in which it grows. The feature which distinguishes the pure adenoma from all



At the operation, the tumor was as large as the girl's fist. Enlarged lymphatic glands were not found in the axilla, and the girl was well two years after the operation.

The second example of this type was a tumor removed from a married woman, aged 34, who had three children. The microscopic appearance of this tumor is shown in figure 27. The tumor consisted of a massive new formation of pathologic adenomatous elements chiefly composed of dilated acini. They may lie in juxtaposition or they may be separated from each other by loose connective tissue. The epithelial elements may consist of a simple layer of cuboidal shaped cells. The cells may pile themselves on the top of one another to form columns three or four cells in height, and the epithelial cells may grow on delicate fibrillous stalks to form papillomas which do not branch. Collections of cells may be sessile (fig. 27).

Clinically, the tumor was growing. The exact pathologic state was not clear at the operation, and the gland was removed as for carcinoma. Microscopic examinations proved that none of the axillary lymphatic glands was affected. The patient was well twenty years after the operation.

other tumors of the breast is that it consists only of a massive new pathologic formation of ducts and acini. The new formation of ducts (fig. 25) may be more excessive than the new formation of acini (fig. 27) and vice versa. I do not know whether this tumor can become malignant. I have seen only two examples. One was a tumor and part of a breast from a girl, aged 15 years (fig. 25). The tumor was composed of a massive new formation of pathologic adenomatacous elements in which formation of new ducts predominated. Within the ducts papillomas had grown (fig. 26). The elastica was continued from the



organism into animals has produced lesions in the colons of rabbits and dogs in all essentials like those found in man. Thus, the disease has been established as an infection of the colon, and for want of a better term the original designation of chronic ulcerative colitis or colitis gravis has been retained.

The infection of the colon is severe and carries with it serious complications and sequelae, such as polyposis, perforation, stricture, hemorrhage, perirectal fistula and abscess, endocarditis, splenomegaly, mesenteric thrombosis, ocular phenomena, tetany, severe anemia, arthritis and malignant disease. The malignant condition, although not common, is undoubtedly the one most dreaded.

In the records of the Mayo Clinic from 1916 to 1927, inclusive, I noted reports of twenty-three cases of chronic ulcerative colitis in which it was believed, because of various clinical and pathologic signs and symptoms, that a malignant disease of the colon had developed. Post-mortem examination in three of these cases failed to reveal malignant disease. There was, instead, extensive ulceration and polyposis. In three others the proof was large filling defects in the colon, with sudden and rapid change of symptoms, obstruction, cachexia and anemia. A specimen for diagnosis was not obtained. In the remaining seventeen cases the condition was proved to be malignant, either by the specimen removed or at necropsy.

I shall include in my discussion, therefore, twenty cases of malignant disease, the seventeen in which the condition was proved by examination of tissue and the three in which it was proved by clinical diagnosis. The age incidence in these cases is significant. Whereas five patients had attained the age of 50 or more, the other fifteen were between 21 and 45 (three were aged 21, 23 and 26 years, respectively; six were between 30 and 39; six were between 40 and 45). Only one patient (a woman, aged 53) gave a history of malignant disease in the family: two uncles had had carcinoma. Nineteen patients were white; one was a mulatto. Fourteen patients were farmers; one was a laborer, one a railroad conductor, one a lawyer, one the wife of a physician, and two were bookkeepers. Symptoms of chronic ulcerative colitis were complained of for from three months to thirty-five years before admission. Only one patient had had symptoms for thirty-five years; the average duration of symptoms of the other nineteen was six years.

The medical treatment had varied, as is usual in these cases. In a few cases, injections of vaccine had been given subcutaneously; in most of them, rectal irrigations with one or another of the so-called intestinal antiseptics had been given.

In most of the cases, a fairly definite change of symptoms could be elicited by which the beginning of the malignant process could be esti-



## REPORT OF ILLUSTRATIVE CASES

**CASE 1.**—A boy, aged 9 years, first came to the Mayo Clinic in 1915. He had suffered with diarrhea for a year or longer, and was passing from five to six stools a day which contained much blood, mucus and pus. As he lived only twenty miles from Rochester, he visited the clinic during the following ten years whenever the trouble became severe, which was several times each year. On his first visit he was placed on treatment for amebiasis, which consisted of emetine, hydrochloride, administered hypodermically, and irrigations of coal-oil. Repeated examinations of the stools did not reveal amebas or parasites of any kind. A diagnosis of colitis was made proctoscopically. Every cold caused an exacerbation of the colitis, and the patient had colds and tonsillitis at all seasons of the



Fig. 1 (case 1).—Roentgenographic appearance of the colon after a barium enema in 1924.

year. Finally, in July, 1924, he was brought to the clinic in an exhausted condition with severe bronchitis and had to be taken to the hospital at once. At this time he said that as long as he could remember he had never passed fewer than six or eight stools in twenty-four hours and that they were always mixed with blood. For weeks after he had a cold, he passed from fifteen to twenty-five stools in twenty-four hours, with severe cramps and tenesmus before and during each passage.

Successive examinations of the stools for endamebas and acid-fast bacilli again gave negative results, but by culture of the scrapings from the bases of the ulcers many gram-positive diplococci were found. The patient had a low grade fever and the maximal leukocyte count was 19,300. The proctoscope revealed active ulcerative colitis, graded 4. Roentgenograms of the colon showed that it was shortened and tubelike (fig. 1). The patient had the pasty appearance of a





CASE 2.—A man, aged 26, came to the Mayo Clinic on Oct. 2, 1925. He said that about ten years previously he began to have bloody purulent rectal discharges with frequent watery stools. At first this occurred at intervals with remissions. In 1917, he was well enough to be admitted to the army, although he did not tell the members of the examining board of bowel trouble. While in the army he spent most of his time in the hospital, a severe exacerbation having occurred in 1917. He passed from twenty to twenty-five bloody stools daily, many of them at night. He had been discharged from the army partially disabled and was well until 1922. From then until his admission into the clinic, diarrhea had been continuous, and his vitality was low. During these years, an average of from six to eight stools was passed a day. He had lost 15 pounds (6.8 Kg.) in the last two years; his weight on admission was 128 pounds (58.1 Kg.).



Fig. 3 (case 1).—Same section as that shown in figure 2;  $\times 340$ .

Pus and blood were found in excess in the stools. Parasites, ova and acid-fast bacilli were not found. The culture yielded the usual diplococcus. On October 2, the hemoglobin was 45 per cent; erythrocytes numbered 3,680,000. The tonsils were septic, and three teeth contained periapical abscesses. Perirectal excoriation, a draining fistula on the right and an anorectal stricture, which barely admitted the index finger, were present. The Wassermann reaction of the blood and the urinalysis were negative. Roentgenograms of the chest, kidneys, ureters and bladder were negative. Roentgenograms of the colon showed narrowing and shortening but no haustra (fig. 4). Proctoscopic examination disclosed a granular ulcerative process, resembling a polyp, and a stricture from 2 to 3 cm. from the anus.

Treatment consisted of a filtrate of the diplococcus, administered subcutaneously, tincture of iodine, 12 minims (0.74 cc.) three times a day, and instillations of witch-hazel daily. The patient improved steadily, and on October 24,



pain was relieved by bowel movement. Two years previously the diarrhea became more severe, and there was more blood and pus; for about six months before admission the pain had been more constant, and the patient had lost 32 pounds (14.2 Kg.). From six to fifteen stools were passed in twenty-four hours. The more he ate the worse the pain became.

After a thorough investigation, a diagnosis of chronic ulcerative colitis was made, and the "Brown operation" and appendectomy were performed. The ileum was severed completely, and the proximal loop only brought out. The patient returned in 1919 much improved, having gained 30 pounds (13.6 Kg.), but he considered the ileostomy opening a nuisance because the prolapse kept him from working. A no. 1 ring pessary was inserted, which seemed to control the prolapse.



Fig. 5 (case 2).—Section of one of the many hyperplastic islets of mucosa disseminated throughout the colon and removed at necropsy;  $\times 75$ .

In February, 1920, the proctoscopic examination showed a stricture 5 cm. above the anus, so small that the lumen could not be seen. The mucosa showed that the colitis was still active, although the patient was clinically in a fair condition.

The patient secured a job as a taxi driver and supervised his farm. He returned in 1925 in good physical condition, weighing 178 pounds (80.7 Kg.). The stricture in the rectum would not admit the index finger. The ileostomy opening with the aid of the pessary was functioning well. He returned home and was in fair health until about the middle of September, 1927, when the sanguinopurulent rectal discharge increased greatly and at the same time a dull, aching, steady pain



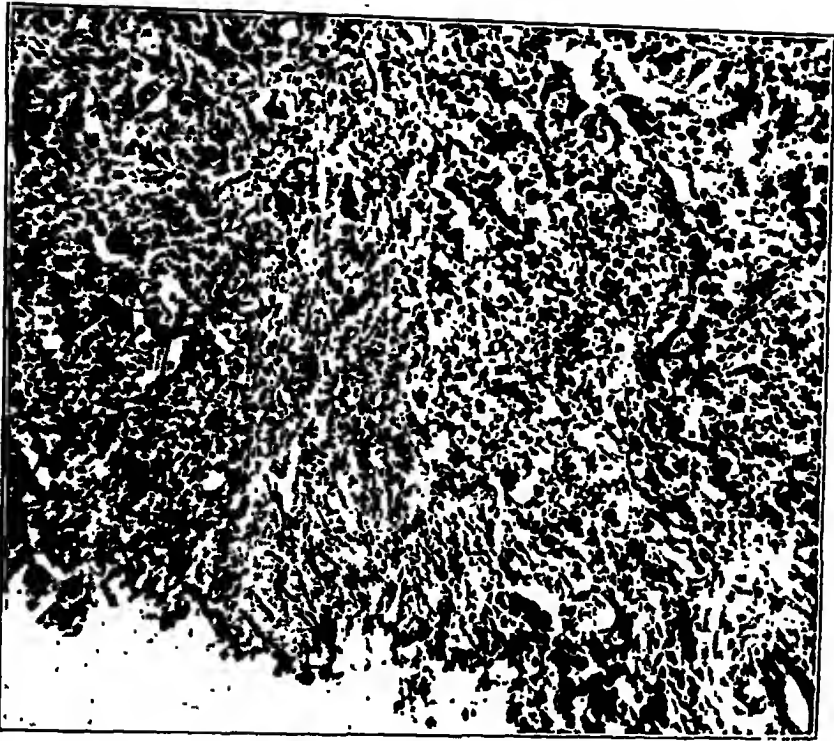


Fig. 7 (case 3).—Section of one of the numerous nodular excrescences of the rectal mucosa removed for diagnosis;  $\times 150$ .

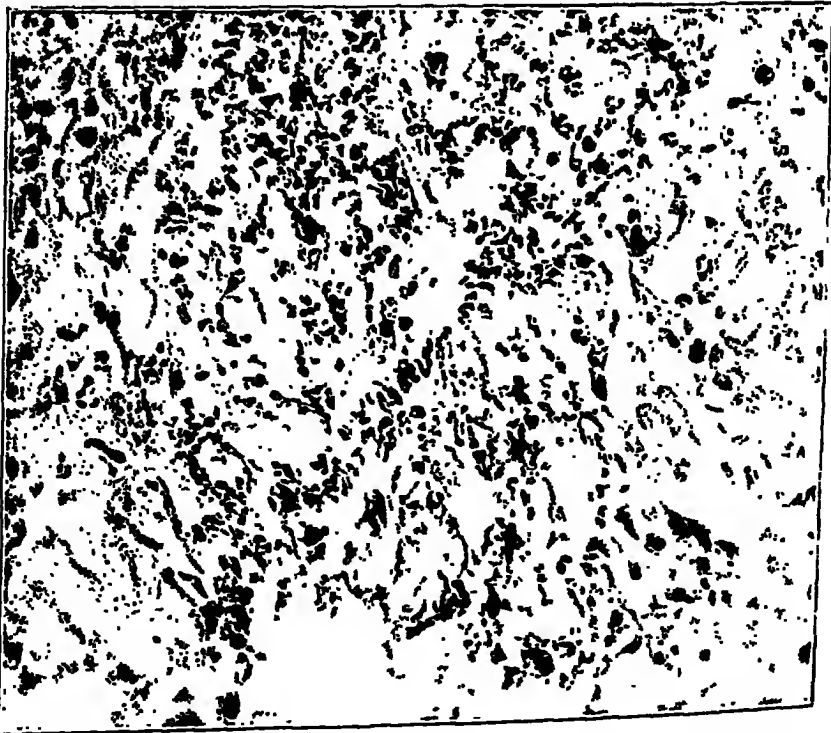


Fig. 8 (case 3).—Same section as that shown in figure 7;  $\times 340$ .

developed at the lower end of the rectum. This became severe in a few days and persisted until his admission to the clinic on December 15. He complained of shooting pains in the genital region, frequency of urination and much difficulty in voiding.

The patient was now 51 years of age. He weighed 158 pounds (71.7 Kg.). The facial appearance was of one in distress. The leukocytes numbered 12,400, and polymorphonuclears, 79 per cent. Proctoscopic examination under regional anesthesia showed the rectal surface to be covered with a grayish, foul-smelling slough, with many irregular areas protruding here and there as far as could be seen. Proctoscopy could not be carried further than 14 cm., because of the limitation of motion and narrowing of the lumen. A specimen of one of the many irregular

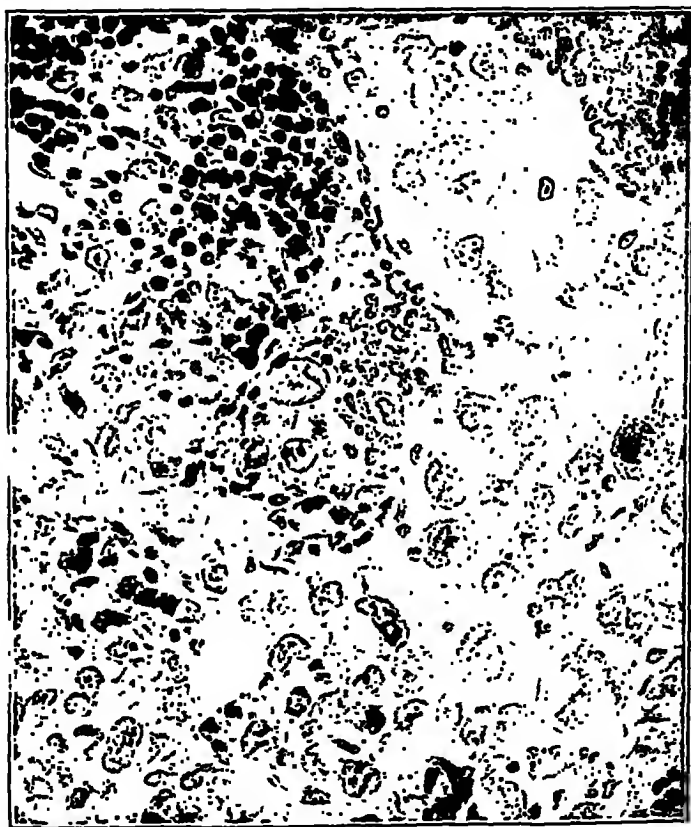


Fig. 6 (case 2).—Same section as that shown in figure 5;  $\times 325$ .

nodules proved to be adenocarcinoma, graded 3 (figs. 7 and 8). The first phalanx of the index finger was inserted into the rectum, and the mucosa felt rough and stiff. The patient is receiving radium treatment elsewhere.

**CASE 4.**—A youth, aged 19, first came to the Mayo Clinic on June 28, 1916. He had been passing loose, watery stools containing flecks of blood for nine years. Proctoscopic examination showed granular proctitis. A roentgenogram of the colon was negative. The hemoglobin was 76 per cent. On his return to the clinic on August 21, roentgen-ray examination showed the colon to be thickened and contracted. Achlorhydria was present. From 1916 to 1920, he got along fairly well, with the exception of periods of frequency of urination, the urine containing blood and mucus. In the first ten years of his trouble, he had had several

patient died on September 20. On this day the blood urea was 252 mg. for each hundred cubic centimeters. Necropsy revealed carcinoma of the transverse colon (figs. 10 and 11), metastasis, chronic ulcerative colitis, generalized peritonitis and multiple infarcts in the lungs. The ulcerative colitis was not active, the mucosa being smooth and shiny, with a suggestion of many healed scars.

CASE 5.—A man, aged 40, came to the Mayo Clinic on Feb. 26, 1923, because of diarrhea of sudden onset two years previously. The rectal discharges averaged from three to fifteen every twenty-four hours. The stools were soft and were mixed with blood and mucus. There was considerable flatulence, and some tenesmus and cramps preceding each bowel movement. The diarrhea was more severe in the afternoon and at night. An acute cold in January had made the diarrhea much worse.



Fig. 10 (case 4).—Section of the tumor which was removed at necropsy and which corresponded to the filling defect shown in the roentgenogram;  $\times 75$ .

At examination, the Wassermann reaction of the blood and the urinalysis were negative. The leukocytes numbered 10,700. Three teeth with periapical infection and somewhat enlarged tonsils were noted. A roentgenogram of the chest was negative. A roentgenogram showed the colon to be smooth and without haustra. Proctoscopic examination showed rather mild activity in the colon, with greater activity in the sigmoid. Parasites or ova were not found in the stools. A diagnosis of chronic ulcerative colitis was made. Tincture of iodine was given by mouth, and a mild solution of protargin and witch-hazel were given by rectum. On March 26, proctoscopic examination did not show improvement. The patient was dismissed, and the condition of the bowels continued as before until Dec. 20, 1926, when, following the lifting of a heavy grain sack, excruciating pain appeared in the right lower quadrant. This continued for two weeks, during which the patient was disabled. The temperature was taken and found to be between 99

hemorrhages and became anemic. Intermittent distress at the umbilicus was relieved by bowel movement. He did better on a full diet. In 1920, he had had influenza, after which the condition became somewhat worse. In 1924, the distress increased and bowel movements were more frequent. After a trip south in April, 1927, the urgency and frequency of bowel movements increased, and he went to Battle Creek Sanitarium where he was placed on a vegetable and fruit diet. After this, emetine and stovarsol had been given, but without improvement. In June, the pains became so severe that he "couldn't get his breath." The pain was worse after a bowel movement; morphine was given for relief. On June 24, a hemorrhage from the bowel occurred. His physician wrote to the clinic for some vaccine which was given during August; blood was believed to have disappeared from the stools after this.



Fig. 9 (case 4).—Roentgenographic appearance of the colon in 1927 showing the typical deformity of chronic ulcerative colitis and a definite filling defect in the transverse colon.

At examination, September 7, the hemoglobin was 60 per cent, the erythrocytes numbered 4,600,000, and the leukocytes, 6,100. The chief complaint was that of intermittent severe attacks of pain in the upper part of the abdomen which was relieved by morphine, of which he had as much as 3 grains (0.195 Gm.) daily. Proctoscopic examination showed chronic ulcerative colitis, graded 2. A roentgenogram of the colon after an enema of barium showed ulcerative colitis of the entire colon with a filling defect from a constriction of the transverse colon (fig. 9). The urine showed hyaline casts, graded 4, and pus, graded 1.

On September 9, ileostomy was performed for carcinoma of the transverse colon and metastasis to the pelvis. After a stormy postoperative course, the



every twenty-four hours. Between April 7 and 11, five deep muscular injections of immune horse serum<sup>12</sup> were given, that is, 10, 15, 15, 15 and 15 cc. were given on successive days. After this, the temperature receded and after April 12 did not go above 99 F. The patient improved gradually and was dismissed on April 17, weighing 113 pounds (51.3 Kg.). He was advised to take the filtrate prepared



Fig. 12 (case 5).—Specimen removed surgically.

from the diplococcus every four or five days, and kaolin if he needed it. At this time he was having from four to six daily bowel movements without blood. On June 6, he had gained 16 pounds (7.3 Kg.), was having three or four daily bowel

12. Rosenow, E. C., and Bargen, J. A.: Unpublished data.

and 101 F. He returned on Jan. 5, 1927. A tender, firm, nodular mass in the right lower quadrant was fairly adherent to the structures around it. Proctoscopic examination at this time showed typical chronic ulcerative colitis, graded 2. The roentgenogram showed that the bowel did not contain haustra, but there was a filling defect in the cecum. The tonsils and infected teeth had not been removed. *Trichomonas hominis* was found in the stools. A culture from the ulcers in the bowel yielded the usual diplococcus. The hemoglobin was 57 per cent, and the leukocytes numbered 12,100. The patient had lost 17 pounds (7.7 Kg.) in a few weeks.

On January 13, ileocolostomy was performed for a cecal tumor which appeared malignant and was surrounded by inflammatory tissue. The adjoining glands were enlarged. Following a fairly uneventful convalescence, four deep exposures of roentgen rays were given as part of the treatment. The patient was dismissed

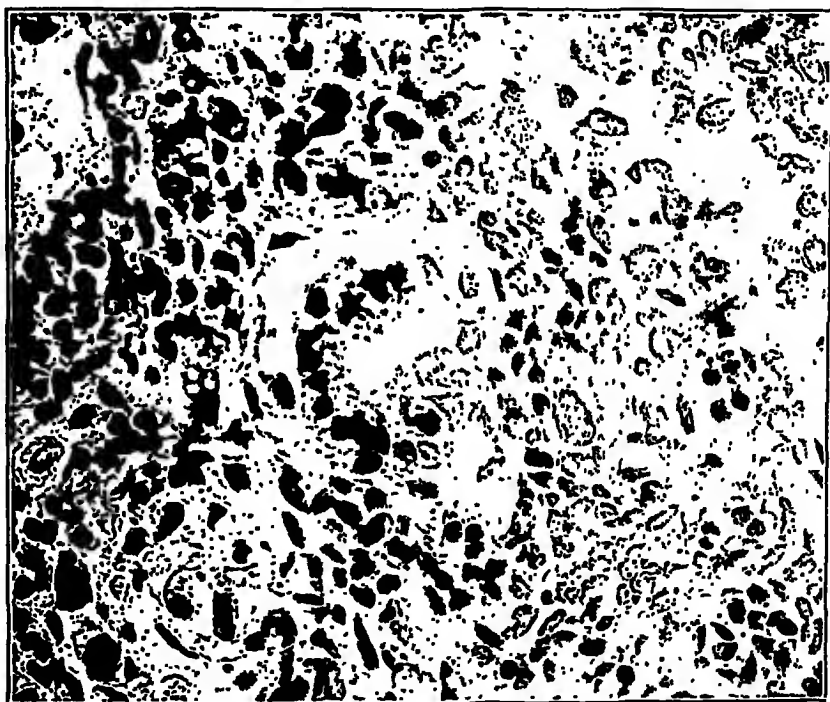


Fig. 11 (case 4).—Same section as that shown in figure 10;  $\times 450$ .

from observation on February 10, and was instructed to take an autogenous vaccine every five days. The rectal bleeding stopped; the weight increased from 119 to 131 pounds (54 to 59.4 Kg.), and when he returned on March 16, he felt well except for pain in the region of the tumor. On March 18, the ileocecal coil was resected, including the large tumor which the pathologist reported to be ulcerating lymphosarcoma of the cecum, without glandular involvement (figs. 12, 13 and 14). A stormy postoperative course followed; pneumonia developed and later, peritonitis. On March 21, 13 cc. of 1 per cent of mercurochrome-220 soluble was given intravenously; this was repeated two days later. The temperature, which before had remained between 103 and 104.5 F. for several days, fluctuated from 101 to 102 for the next two weeks. Following the injection of the mercurochrome, the bowels became much more active; from ten to thirteen bloody stools were passed

movements and was feeling well. Roentgen-ray treatment was again administered. He got along well, and then discontinued the vaccine early in September. On October 25, he wrote that he was having a further upset of the bowels, from nine to ten stools without blood being passed daily. A report in March, 1928, stated that he was in good condition.

## COMMENT

The paucity of reports in the literature on malignant disease of the colon developing in persons with chronic ulcerative colitis is noteworthy. Struthers<sup>13</sup> emphasized the relationship of chronic ulcerative colitis and polyposis, and suggested that malignant disease may follow these conditions. Hewitt and Howard<sup>14</sup> made similar observations. Wheeler<sup>15</sup> expresses the belief that polyposis occurs as a result of chronic ulcerative colitis. Helmholz<sup>16</sup> called attention to the fact that Virchow and Rokitsansky may have described the terminal stage of chronic ulcerative colitis. Soper's<sup>17</sup> work on multiple polyposis of the colon has been illuminating. At the Mayo Clinic the development of polyps has been noted proctoscopically in the course of progressing as well as healing chronic ulcerative colitis. Logan<sup>18</sup> found polyps in 19 of 117 cases. Later, I noted 26 in 200 cases.

In view of the various reports in the literature, the frequency with which polyposis has occurred in the series of cases of chronic ulcerative colitis at the Mayo Clinic and the simultaneous occurrence of polyps and carcinoma in the diseased colon, the following hypothesis is offered: the sequence of events in some cases of malignant disease of the colon is chronic ulcerative colitis, multiple polyposis and malignant disease.

Malignant disease superimposed on chronic ulcerative colitis offers a grave prognosis. Whenever a sudden change for the worse is noted, further proctoscopic and roentgenologic investigations should be made. Operation, even if the malignant condition is discovered fairly early, yields discouraging results. One must then consider medical treatment. The only hope, it seems, is preventive treatment, that is, the cure of the colitis and the removal of the polyps.

13. Struthers, J. E.: Multiple Polyposis of the Intestinal Tract, *Ann. Surg.* 72:649, 1920.

14. Hewitt, J. H., and Howard, W. T.: Chronic Ulcerative Colitis with Polyps: A Consideration of the So-Called Colitis Polyposa (Virchow), *Arch. Int. Med.* 15:714 (May) 1915.

15. Wheeler, W. I. de C.: Multiple Polypi of the Colon, *Brit. J. Surg.* 14:58, 1926-1927.

16. Helmholz, H. F.: Chronic Ulcerative Colitis in Childhood, *Am. Jour. Dis. Child.* 26:418 (Nov.) 1923.

17. Soper, H. W.: Polyposis of the Colon, *Am. J. M. Sc.* 15:405, 1916.

18. Logan, A. H.: Chronic Ulcerative Colitis: A Review of 117 Cases, *North-west Med.* 18:1, 1919.



Fig 13 (case 5).—Section of specimen showing in figure 12;  $\times 75$ .

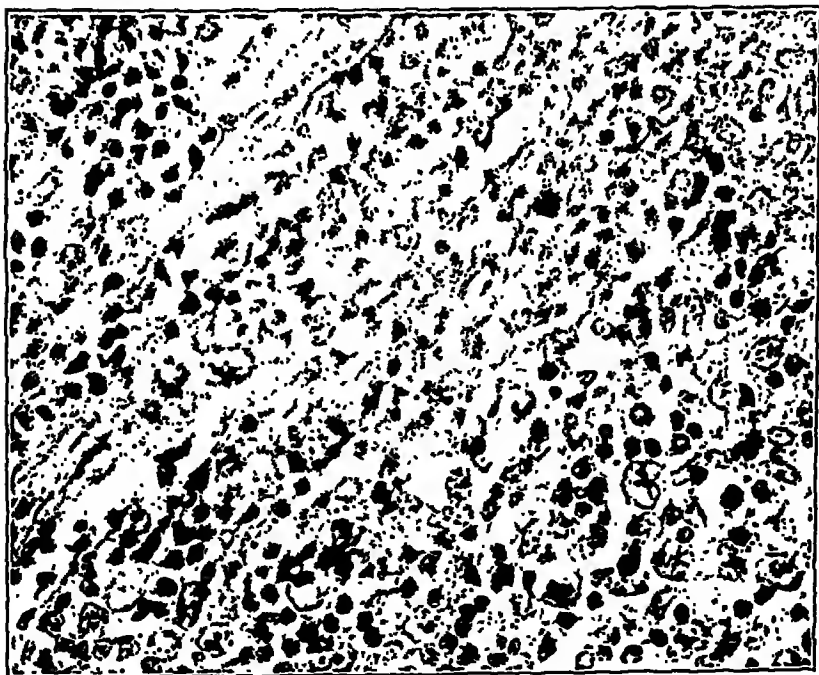


Fig. 14 (case 5).—Same section as that shown in figure 13;  $\times 350$ .

flask containing the mass for injection which has been kept in the lower chamber. This mass is forced into the vessels until the mercury in the manometer remains constant at 150 mm. without requiring additional compression. The vessel is then tied off, the cannula removed, and the appendix immersed in cold formaldehyde for fixation and bleaching, after which an x-ray picture is made. After fixation, the appendix is gradually dehydrated in alcohol commencing with 50 per cent and changing every alternate day into an alcohol of 10 per cent additional strength until absolute strength is attained. The appendix is then immersed in synthetic oil of wintergreen, and within two days clearing is complete. The finest branches are clearly visible, dissection being rendered simple. The serosa and, separately, the muscularis can be peeled off, and with the aid of an ordinary hand glass, the distribution, direction and anastomosis of even the finest branches are easily studied.

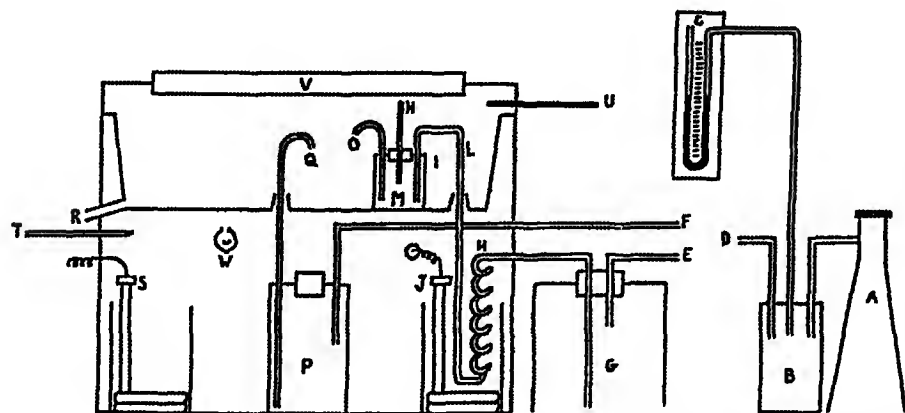


Fig. 1.—Injection apparatus. *A* indicates the compressed air tank which blows air into *B*, the chamber which registers the air pressure by means of manometer *C*. *D* is the pressure tube which can be attached to either *E*, the inlet tube of the physiologic sodium chloride flask, or *F*, the inlet tube of the injection mass bottle. By this means, the sodium chloride solution can be forced out of the flask *G* into the spiral tube *H*, which is being heated by the immersible electric heater, *J*. The sodium chloride solution is thus forced out of the spiral *H* through the tube *L* into the bottle *M*, where the temperature is registered by the thermometer *N*. Tube *O* conducts the sodium chloride solution through the cannulae to the organ. Similarly, by applying pressure tube *D* to *F*, the injection mass can be forced out of bottle *P* through *Q* into the cannula. *R* is the outflow tube; *S*, another immersible electric heater; *T* and *U*, the thermometers for registering the temperature of the chambers; *V*, the glass window for observing the condition of the injecting organ; *W*, an electric illuminating bulb (organ for injection is suspended from a tripod in the upper chamber). (From L. Gross: Blood Supply to the Heart.)

The mass of barium sulphate gelatin is made as follows: Soak 300 Gm. of fine French gelatin (preferably gold label) for two hours in 1,200 cc. of distilled water. To this add 1,000 Gm. of finely powdered

# THE BLOOD SUPPLY TO THE APPENDIX \*

HARRY KOSTER, M.D.

Attending in Surgery

AND

MORRIS WEINTROB, M.D.

Assistant in Surgery, Crown Heights Hospital

BROOKLYN

This paper is based on the study of the arterial architecture of 100 appendixes, normal and pathologic, removed from human beings representative of the first to the seventh decades of life, inclusive. The method pursued in the study was originally described by Louis Gross in his work on the blood supply to the heart. This consists, in brief, of the injection of the appendicular artery with a barium sulphate-gelatin suspension of known viscosity. The injection is accomplished in an apparatus which permits accurate control and standardization of temperature, pressure and other modifying elements.

The apparatus consists of a wooden box lined with copper and separated into two chambers, an upper and a lower chamber, by a pan which has an outflow tube connecting it with the outside. In the center of the pan are two openings, nicked to prevent dripping into the lower chamber (fig. 1). Outside the incubator is a Wolff flask. Compressed air is forced into this flask until an attached mercury manometer registers 150 mm. of mercury. The pressure tube from this bottle is connected to a large flask containing physiologic sodium chloride solution. The solution is forced out of the flask into a spiral tube in the lower chamber which is immersed in a bath kept warm by an electric immersion heater. The physiologic sodium chloride solution is then conducted into the upper chamber into a small Wolff flask which contains a thermometer. The temperature of the solution is thus accurately determined before it is forced into the blood vessels. By raising or lowering the spiral tube in the water bath, the temperature can be altered to any degree desired, and the sodium chloride solution at the proper temperature is then forced through the appendicular artery until the washings come clear. The entire incubator is kept at a uniform heat by another immersion electric heater, a thermometer being placed in each chamber. Electric bulbs and glass doors render it easy to watch the progress of the injection. When the blood vessels are washed clean, the pressure tube from the manometer bottle is attached to a Wolff

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\* From the surgical service of the Brownsville and East New York Hospital, Brooklyn.

triangle, the apex of which is the distal appendicular end. In a percentage of cases, the artery instead of terminating at the tip of the appendix rounds the extremity and is continued on the free border of the organ as a "backbone" vessel which extends for a distance of approximately 2 cm. As will be seen later, this "backbone" vessel at this point receives numerous anastomoses.

In its arcuate course, the appendicular artery in the average case gives out seven primary branches. These extend at right angles to the trunk artery and are approximately equidistant and parallel to one another. With the exception of usually the first, all primary branches divide into two encircling branches at a distance of about 5 mm. before reaching

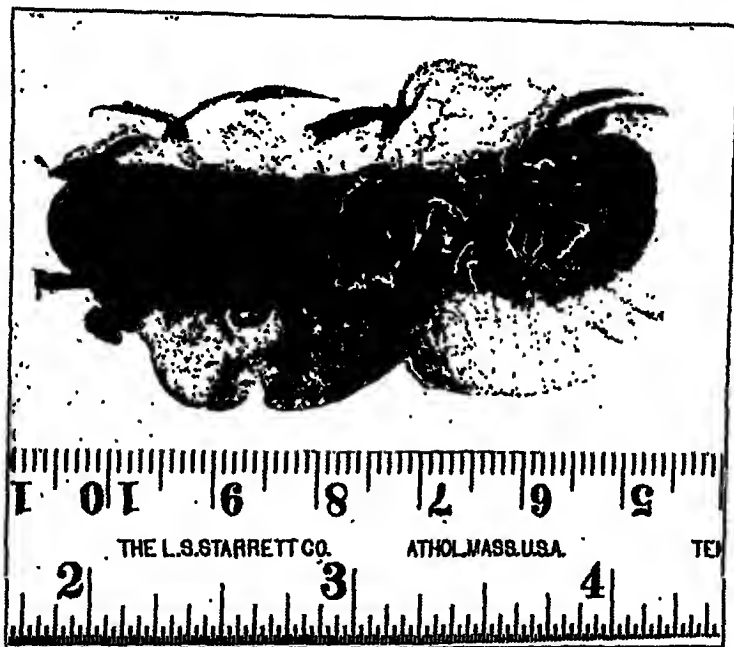


Fig. 3.—Serosa dissected free from underlying coats. Note the fine caliber of the vessels in comparison with the larger vessels of the submucosa.

the appendix. The first primary branch differs in that the secondary branches are given off before encircling branching occurs (fig. 2).

The encircling branches almost immediately break up into two layers, a deep and a superficial, which dichotomize extensively and surround the appendix with tortuous interanastomosing vessels. The superficial layer of vessels runs in the serosa and, much to our surprise, they are of noticeably smaller caliber than those of the deeper layer. The latter distribute themselves in the submucosa. There is apparently no distinct supply to the muscular layers (fig. 3).

Obviously, the caliber of the encircling vessels diminishes as branching proceeds and as the free border is approached. The latter fact

barium sulphate, 500 cc. of distilled water and 2 Gm. of thymol. Heat over a water bath until the gelatin dissolves and the whole mass becomes a homogeneous milky fluid. Filter through two layers of Victoria lawn.

To secure specimens suitable for injection, i. e., the appendix and all of the meso-appendix as far back as the trunk of the appendicular artery before branching begins, the ordinary procedure in the operation of appendectomy had to be modified. The method employed is to pass a suture ligature around the vessel as it enters the base of the meso-appendix on its free border, ligate and then cut free to the base of the appendix. The appendicular base is then ligated and cut distally by the cautery at dull heat. The heat sears the free end, preventing spill, and obviates the undesirable use of a clamp which would injure some part of

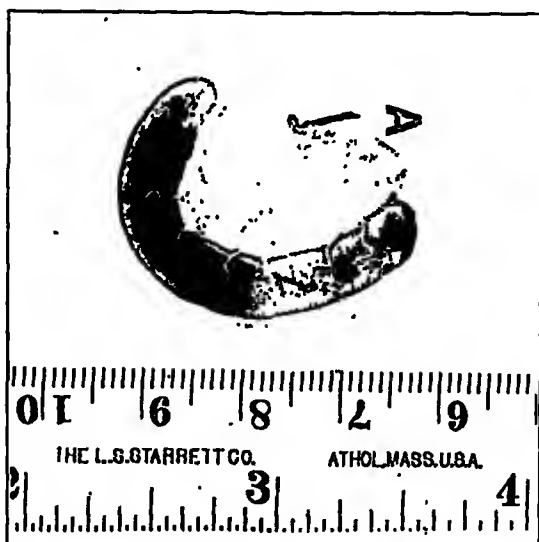


Fig. 2.—Normal appendix. Note the secondary branching, tortuosity, encircling branches and the diminution in their size as they approach the free border of the appendix.

the vasculature. The appendix is placed in citrated saline to prevent coagulation in the vessels. A fine glass cannula is then tied into the artery, and the specimen is ready for injection.

#### CIRCULATION IN THE NORMAL APPENDIX

The appendicular artery arises from the ileocolic artery and enters the base of the meso-appendix at its free border. Usually, this location is marked by the presence of an easily demonstrable gland which, incidentally, is the first to show the presence of an inflammatory lesion in the appendix. This vessel pursues an arcuate course along the free border of the mesentery, approaching the appendix as it extends toward the tip, thus forming with the appendix approximately an isosceles



Microscopic study results in the confirmation of many of these gross observations. It is apparent that there is a much larger and a much more profuse vascular supply to the submucosa than there is to the serosa. Examination of serial sections in the process of the construction of a wax model for the more accurate study of the arterial tree confirmed the belief that a distinct blood supply peculiar to the muscularis is absent. Where blood vessels are seen in the muscularis they are small, right angled, connecting vessels which span the gap between the superficial serosal and the deep submucosal layers and in so doing pass through a "defect" in the musculature, the so-called hiatus-muscularis. From the large vessels in the submucosal layer, fine vessels run toward the mucosa. These vessels are quickly lost sight of as they reach the mucosa. On the whole, the formed vascular supply in the area of the lymph follicles is scant. The follicles are, however, generously supplied with lymphatic vessels. It would seem from this distribution as though the absorption from the lumen of the appendix would be primarily and mainly by way of the lymphatics rather than directly into the blood stream—unlike the arrangement in the jejunum and ileum (fig. 5).

#### CIRCULATION IN THE PATHOLOGIC APPENDIX

The pathologic appendixes which we have examined resolve themselves into four groups: (a) early exudative appendixes, in which gross evidence of inflammation is not striking; (b) marked exudative appendixes, in which though the tissue layers do not as yet show macroscopic evidence of necrosis, definite, easily demonstrable evidence of acute inflammation is seen; (c) well marked suppurative hemorrhagic and necrotic appendixes in which the necrotic lesion has not, however, led to extensive gangrene, and (d) gangrenous appendixes in which considerable portions of the organ are seats of ischemic necrosis.

The changes in the vascular picture which accompany the various phases in the transition from normalcy through the grades outlined in the foregoing paragraph (obviously artificially and arbitrarily outlined) parallel closely the general pathologic condition of the organ. Thus, one finds appendixes belonging to category (a) which show scarcely any macroscopic deviation from the normal in their blood supply.

One of the earliest visible changes in the arterial tree is a diminution in the tortuosity of the larger branches in the two layers (deep and superficial). Usually concomitant with this, and often apparently in direct proportion to the extent of this diminution, is an increased prominence of the rami telae adiposae. As the organ becomes more swollen and the inflammatory lesion more marked, the larger branches completely lose their tortuosity; at the same time, the radial vessels communicating between the two layers become increasingly prominent. The

may be of interest in connection with the frequency with which perforations occur at this site.

The description thus far given deals with the vessels of larger caliber. In their distribution, these branches give off a tremendous number of delicate vessels which turn abruptly at right angles to their course, run in a radial direction, and bring about a profuse anastomosis between the branches of the deep and superficial layers. They pass through a hiatus in the musculature, which is readily seen on microscopic section. This system of delicate radial vessels is excellently demonstrated in edematous appendixes, in which the two layers mentioned are more sharply defined and separated.

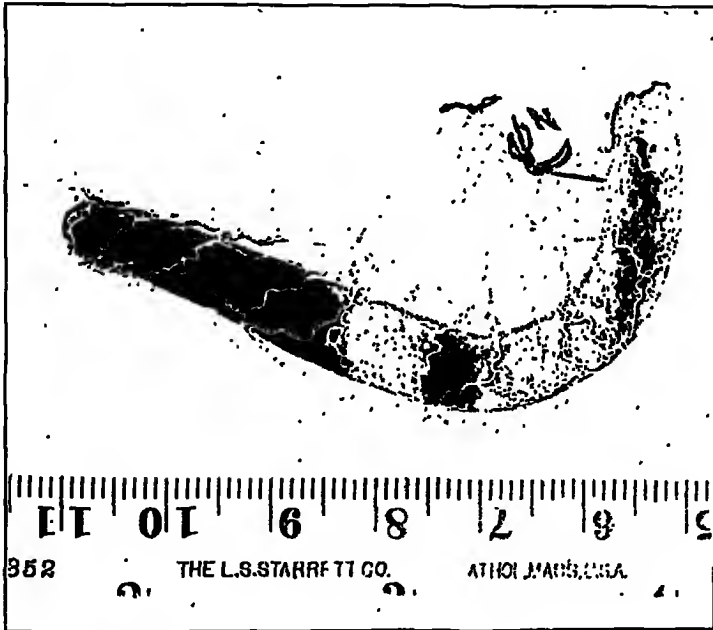


Fig. 4.—Normal appendix. Note the tortuosity of the vessels and the fine vessels in the fat layer, the rami telae adiposae.

The next group of vessels we believe to be of considerable physiologic importance is that system of delicate interlacing and interanastomosing vessels found in the fat of the meso-appendix. These fine vessels (rami telae adiposae) arise from the appendicular artery as well as from its branches in the meso-appendix, interanastomose freely in the fat of the meso-appendix and, as in other organs in which these vessels are found, e. g., the heart, kidney and other organs, often accompany larger branches. As will be noted in the subsequent description of the circulation of the pathologic appendix, these fine vessels apparently play an important rôle in compensating for obliterated or thrombosed vessels (fig. 4).

relation between the inflammatory edema, on the one hand, and the diminished tortuosity and increased prominence of the radial communicating vessels, on the other, is so definite that the microscopic picture of edema and inflammation can be accurately predicted from the gross examination of the vessels in the cleared appendix (fig. 6).

Following this stage, one of the most conspicuous additional changes consists in the abrupt termination of the lumen of the vessels, often at points where the caliber has not yet appreciably diminished, that is, at considerable distance from their estimated ultimate distribution. This marks the transition to the development of gangrene in the tissue (fig. 7).

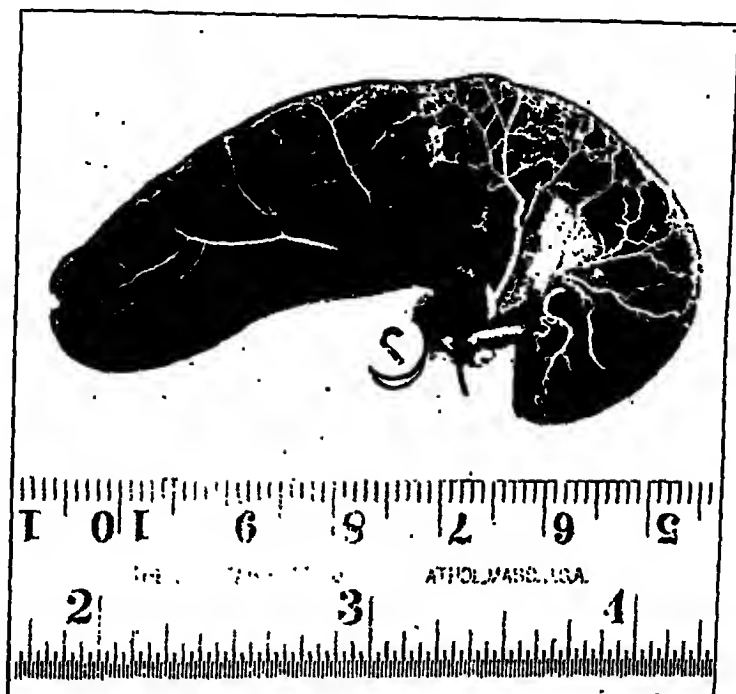


Fig. 6.—Acute suppurative appendicitis. Note the diminution in tortuosity and the greater prominence of the vessels.

Finally, in the specimens representative of category (*d*) is seen complete absence of blood supply to the affected portions. It is of interest to note that when these ischemic areas involve only part of the entire organ, they are most frequently seen at either the proximal or the terminal portion of the appendix, usually the latter. We have not yet encountered ischemic necrosis involving only the middle portion of the appendix.

Microscopic study confirms the gross observations. In the early exudative cases, the only vascular changes noted are increased prominence of the capillaries and apparent distention of the larger vessels.

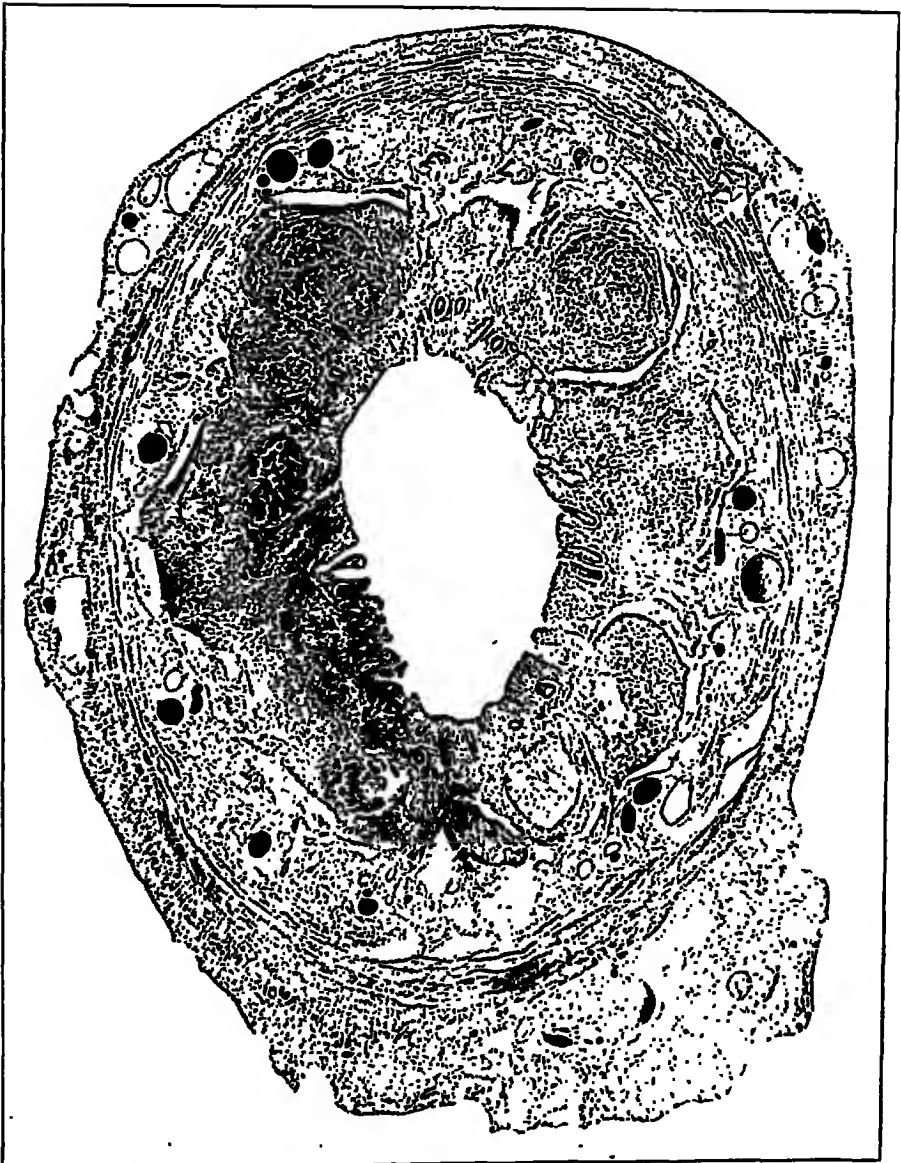


Fig. 5.—Microscopic section of a normal appendix. The dark, ovoid areas are cross-sections of the injected vessels. Note the difference in size and profusion of the vessels in the submucosa as compared with these in the serosa, and the relative paucity of formed vessels in the mucosa. The vessels seen in the muscular layer merely traverse it, as shown by serial sections.

The definite determination of the supply into two layers, the richer of which is the deeper, and the absence of a distinct blood supply to the mucosa, are undoubtedly of physiologic importance. Attention is again drawn to the remarkable corkscrew and spiral character of the appendicular branches of the second, third and subsequent orders. From analogy with other organs in which this type of vessel is found, e. g., the uterus, intestine, urinary bladder, etc., this tortuosity speaks for a structure which is constantly changing in shape and in caliber.

The next striking point about the blood supply is its richness and profuse anastomosis. This, again, is analogous to the condition found in organs subject to vascular obliteration, e. g., the heart. The number of fat vessels found in the meso-appendix seems to be out of proportion to that necessary to nourish a similar amount of fat, and the close parallelism between the prominence of these vessels and the extent of the inflammatory process in the appendix suggests that these vessels play a compensatory rôle.

It has been shown that inflammations of the appendix are consistently paralleled by changes in the course and character of the blood vessels. Undoubtedly, most of these changes follow the original inflammatory changes and are due to the edema. Another study is under way to determine whether a primary vascular lesion, such as, for example, a bacterial embolus, may not be responsible for at least some of the lesions found in the diseased appendix, and perhaps at times be causally responsible for appendicitis.

The diminution in tortuosity and the increased prominence of the radial twigs are undoubtedly occasioned by the swelling of the appendix and separation of the layers. Vascular obliteration is due to edema and in some instances to thrombi.

It is obvious that at least in those cases coming under categories (a) and (b) in which the vascular changes are only qualitative in nature, restitution to integrity of the organ may follow a subsidence of the inflammation. When, however, the process has proceeded to vascular obliteration to any considerable extent, complete return to normalcy is hardly to be expected.

There remains to be explained the peculiar fact that the middle portion of the appendix is rarely involved alone in an ischemic gangrenous lesion. A satisfactory explanation for this phenomenon has not as yet been found.

In the appendixes of category (b), and more particularly in (c), the rami telae adiposi are prominent, and it seems logical to conclude that their increased size is probably a compensatory and defensive phenomenon.

As the edema increases, not only do the vessels straighten out, but, as a result of the surrounding compression, their caliber diminishes until ultimately (with marked edema) the lumen does not remain patent. Gangrene naturally ensues. The abrupt termination of the lumen of the vessels, often at a point where the caliber has not yet appreciably diminished as previously mentioned, is not always due to the com-



0	1	9	8	2	3	2
2			3			

painful hip was presented by two patients. Pneumonia with empyema, tonsillectomy complicated by aspiration pneumonia and empyema, scarlet fever, acute rheumatic fever, suppurative axillary adenitis and wound infection of the face were the remote sources of infection in the remaining six cases. Cultures of pus obtained from eight of the sixteen patients demonstrated the presence of the following causative agents: *Staphylococcus aureus*, four; *Streptococcus hemolyticus*, two; *Staphylococcus albus*, one; *tubercle bacillus*, two, and *Diplococcus pneumoniae*, one.

The source of the pus in the foregoing cases was from the hip joint, except in two patients. The patient in case 14 developed a metastatic purulent arthritis of the elbow, from which the pus was obtained; in case 12 the pus was obtained from the pleural cavity.

TABLE 1.—Classification of Cases

1. Acute septic arthritis of the hip joint secondary to		
Acute rheumatic fever.....	1	
Infection of the upper respiratory tract.....	5	
Scarlet fever .....	1	
Otitis media .....	2	
Tonsillectomy (aspiration pneumonia).....	1	
Acute osteomyelitis .....	3	
Pneumonia .....	1	
Suppurative axillary adenitis.....	1	
Wound infection of face.....	1	
	—	16
2. Anterior poliomyelitis .....	4	
3. Congenital spastic paralysis.....	4	
4. Chronic infectious arthritis		
a. Polyarticular arthritis (Still's disease).....	2	
b. Tuberculous arthritis .....	2	
	—	12
		28

Four patients presented a dislocation of the hip joint resulting from paralyzes of anterior poliomyelitis involving the muscles surrounding the hip joint. Not only did the residual paralyzes involve the muscles controlling the hip joint, but there were extensive paralyzes involving both lower extremities in three patients, and marked involvement of the dislocated extremity in the fourth patient. The local paralyzes about the hip joint are, as a rule, associated with paralyzes disturbing stability and mobility of the knee and foot; also abdominal paralyzes with resulting spinal curvature and paralyzes of the muscles of the upper extremities may be present. Many of the associated deformities are even more serious lesions than the dislocation, obviously, making the campaign of treatment a complicated problem in certain individual cases. In each of the four patients, the head of the femur could easily be displaced and reduced in the acetabulum by manipulation. Sever<sup>2</sup> reserved the

2. Sever, J. W.: Boston M. & S. J. 165:313, 1911.

# SPONTANEOUS DISLOCATIONS OF THE HIP JOINT DURING EARLY LIFE

REPORT OF TWENTY-EIGHT CASES\*

VERNON L. HART, M.D.

ANN ARBOR, MICH.

Dislocation of the hip joint may be classified as congenital, acquired traumatic and acquired nontraumatic, which is also termed pathologic or spontaneous. From November, 1923, to May, 1928, 103 patients with congenital dislocations of the hip joint, six with traumatic and twenty-eight with spontaneous dislocations have been admitted to the University Hospital. Numerous articles have appeared in the literature concerning congenital and traumatic dislocations; however, comparatively little space has been given to the discussion of spontaneous dislocation of the hip joint, which is undoubtedly more frequent than traumatic dislocation, congenital dislocation being the most frequent type. The incidence of traumatic dislocation would obviously be greater in an industrial center; in general, it is not a common form of injury. Wilson and Cochran<sup>1</sup> state that "traumatic dislocation of the hip joint is an uncommon accident and forms only about 2 per cent of all dislocations. Because the exposure to trauma is greater, it occurs more frequently in males than in females, and usually between the ages of 15 and 50 years." Spontaneous dislocation appears to affect males and females about equally, and usually occurs during the age periods of infancy, childhood and early adolescence. Of the twenty-eight cases included in this report, fourteen occurred in males and fourteen in females, and in all the cases the dislocation occurred before the age of 17 years. There is no record in the university Hospital of a spontaneous dislocation of the hip joint occurring during the age periods of late adolescence, early or late adult life.

## ETIOLOGY

Metastatic septic arthritis of the hip joint, secondary to a remote infection, occurred in sixteen of the twenty-eight cases. Five patients gave a history of infection of the upper respiratory tract, diagnosed as "grip" or "influenza," preceding the involvement of the hip joint. Acute osteomyelitis, with subsequent infection of the hip joint, occurred in three patients. A history of a "discharging ear" soon followed by a

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\* From the Orthopedic Division of the Department of Surgery, University Hospital.

1. Wilson, P. D., and Cochran, W. A.: *Fractures and Dislocations*, Philadelphia, J. B. Lippincott & Company, 1925, p. 457.



Flexion deformities of the hips frequently result during the course of chronic infectious arthritis without the development of dislocation, but if adduction and internal rotation are added to the flexion deformity of the hip joint, dislocation may result. The combination of flexion, adduction and internal rotation may be present without the production of dislocation. Undoubtedly this is due to the insidious onset with the formation of intra-articular and extra-articular adhesions and fibrosis, which aid in maintaining the femoral head in the acetabulum. The dislocated hip in each of the two children was in a position of flexion adduction and internal rotation.



Fig. 1 (case 1).—Spontaneous dislocation of the left hip secondary to acute rheumatic fever.

A positive diagnosis of tuberculosis of the hip joint with posterior dislocation was made in two patients. The attitude of flexion adduction and internal rotation is the usual one in late untreated cases of tuberculosis of the hip joint. Dislocation is unusual, perhaps also due to the insidious onset of the disease and scar formation about the femoral head aiding in the prevention of dislocation. During the acute stage of tuberculous arthritis with muscle spasm, the position of flexion, abduction and external rotation is the rule.

term subluxation for this type and dislocation when the femoral head lies habitually outside of the acetabulum.

An analysis of the function of the muscles surrounding the dislocated hip in the four patients is given in table 2.

A study of the localized paralyses about the dislocated hip joint shows that the extensor, or gluteus maximus muscle, and the abductor muscles, principally the gluteus medius, were either completely or extensively paralyzed, while the flexor and adductor groups were either normal or only slightly involved. It is a physiologic phenomenon that normal unopposed muscle fibers shorten and if maintained in this position will undergo actual structural shortening, resulting in contractures. Without treatment the unopposed flexors and adductors tend to shorten, producing a flexion adduction contracture of the hip joint, which position is productive of dislocation. Each of the four patients presented the flexion adduction contracture deformity of the involved hip.

TABLE 2.—*Function of Hip Muscles*

	Flexors	Extensors	Abductors	Adductors	Tensor Fascia Lata
Case 17.....	Good	Poor	Poor	Good	Good
Case 18.....	Good	Zero	Zero	Normal	Normal
Case 19.....	Normal	Zero	Zero	Good	Fair
Case 20.....	Record not accurate due to lack of cooperation				

Congenital cerebral paralysis with paraplegia was the etiologic factor in four patients. Loss of muscle coordination, with the resulting deformities of adduction of the hip joints, shortening of the hamstring groups of muscles and talipes equinus forms the usual clinical picture in cases of congenital cerebral paralysis with spastic paraplegia. A large group of patients with spastic paraplegia with the foregoing deformities were admitted to the hospital; however, only four developed posterior dislocation of the hip joint. An analysis of the position of the dislocated extremity revealed a flexion internal rotation position, associated with the adduction. Flexion contracture of the hip joint is a frequent occurrence with residual paralyses of anterior poliomyelitis, involving the muscles surrounding the hip joint, without the production of dislocation. However, when adduction and internal rotation are combined with the flexion contracture, dislocation may occur.

Two children were admitted to the hospital with posterior dislocation of the hip joint, complicating polyarticular arthritis or Still's disease. Neither child had been ambulatory during the six years previous to the time of admission. There were numerous joints involved and many associated deformities, which required correction preliminary to any treatment for reduction of the dislocation of the hip joint.

## HIP INVOLVED

Of the twenty-eight cases reported in this paper, three presented bilateral and twenty-five unilateral dislocation of the femoral head from the acetabulum. The unilateral dislocations involved the left hip in sixteen cases and the right hip in nine cases. Twelve of the twenty-five patients had some existing pathologic condition in the hip joint or surrounding groups of muscles of the opposite extremity. In each of the twenty-eight patients, the dislocated extremity was in a position of



Fig. 3 (case 10).—Osteomyelitis of the greater trochanter, femoral neck and upper femoral shaft. Note the position of instability and threatening dislocation of the left femoral head from the acetabulum. The relation between the position of instability and dislocation of the femoral head was not recognized in this case. The position of instability was not changed to the position of stability, and spontaneous dislocation resulted. See figure 4.

flexion adduction and internal rotation, except in case 7, in which the patient entered the hospital with a purulent arthritis of the left hip joint, complicated by dislocation, with an attitude of flexion abduction and external rotation. At operation, the capsule of the hip joint was found to be under marked tension and greatly thinned, due to the pressure of an intracapsular abscess. The pressure of the abscess.

If it is replaced by flexion, adduction and internal rotation, before the formation of considerable fibrosis, then dislocation is imminent. The dislocated extremity in each of the two children was held in the position of flexion adduction and internal rotation.

#### AGE INCIDENCE

The dislocation of the femoral head from the acetabulum occurred in each of the twenty-eight cases before the age of 17 years. Spontaneous dislocation of the hip joint may undoubtedly occur during adult life, although there is no record in the University Hospital of its



Fig. 2 (case 1).—Roentgenogram after preliminary skeletal traction and arthrodesis of the left hip joint. The result is most satisfactory. There is at present a bony ankylosis of the left hip joint in a good position for weight bearing.

occurrence. Hilton<sup>3</sup> recognized that dislocation complicating hip joint disease is usually a condition of early life. He stated that "the acetabulum in a child is very shallow compared with that of an adult. It thus offers greater facility for displacement. This, I apprehend, may be the reason why dislocation of the thigh bone occurs so frequently in cases of hip joint disease at an early period of life."

3. Hilton, J.: *Rest and Pain*, New York, 1879, p. 192.

disease. It is clear that a derangement in the muscle balance is the one pathologic factor common to all cases and should be considered the essential factor in the mechanism of the development of the dislocation.

#### MECHANISM OF DISLOCATION

In a recent paper, R. Watson Jones<sup>+</sup> of Liverpool, clearly demonstrated that the mechanism of the production of the dislocation is a derangement of the normal action of the muscles surrounding the hip joint and is not dependent on lesions of bone or ligament. The normal



Fig. 5 (case 5).—Tonsillectomy complicated, with aspiration pneumonia, metastatic septic arthritis of either hip joint with bilateral spontaneous dislocation and bilateral epiphyseal separation. During the early stage of involvement of the hip joint, the extremities were supported with pillows beneath the knees, placing hips in position of instability.

muscular arrangement about the hip joint may be altered by muscle spasm, muscle paralyse and muscle incoordination. Muscle spasm is always present during the acute phase of hip joint infection, and without treatment the extremity assumes an attitude of flexion, associated with either abduction and external rotation or adduction and internal rotation. One has observed that the most frequent position assumed during the acute stage of hip joint infection is flexion, abduc-

with gradual stretching and thinning of the capsule, forced the femoral head from the acetabulum although the extremity was held in the position of stability.

#### PATHOLOGY

The local pathologic condition of the hip joint varied, depending on the etiologic factor, age of the disease and the period of weight bearing. The pathologic changes of the first group of sixteen patients with septic arthritis of the hip joint varied from a serous to a purulent arthritis with or without destruction of bone and soft tissue.



Fig. 4 (case 10).—The position of instability was not corrected to the position of stability, and spontaneous dislocation resulted.

In each case the normal muscle balance of the surrounding groups of muscles was disturbed owing to muscle spasm during the acute stage of the disease. The second and third groups of patients with involvement of the lower and upper neurone, respectively, obviously did not present any arthritic changes. The local pathologic condition consisted in a disturbance of the normal muscular balance, resulting from flaccid paralyzes of anterior poliomyelitis and muscle incoordination with increased muscle tone as the result of a cerebral lesion. The local pathologic condition in group 4 likewise varied from slight to extensive bone and joint destruction with a disturbance of the normal muscle balance, due to muscle spasm present during the acute period of the



Fig. 7 (case 4).—Suppurative axillary adenitis with metastatic septic arthritis of the left hip joint. Note the position of instability and resulting spontaneous dislocation of the left hip.



Fig. 8 (case 4).—Complete reduction of the femoral head in the acetabulum following skin traction, gradually changing the position of instability to that of stability—abduction and extension.

tion and external rotation, without the production of dislocation. The position of flexion adduction and internal rotation is not infrequent, and it is this group in which dislocation is imminent. The first position is one of stability; the second is one of instability. Regarding the second position, Jones<sup>4</sup> states that "in this position the head of the femur is only partly covered by the postero-inferior rim of the acetabulum—its shallowest rim, so that there is little bony



Fig. 6 (case 5).—Roentgenogram following incision and drainage of abscesses and an attempt to place the extremities in the physiologic position by skin traction. Both sequestrated epiphyses were excised.

obstacle to dislocation. The greater part of the head is in contact with the capsular ligament, which is also comparatively weak at this part (ischiocapsular fibres)." Eleven of the twenty patients included in groups 1 and 4 had bilateral involvement of the hip joint. The extremity in a position of flexion abduction and external rotation was

4. Jones, R. W.: *Brit. J. Surg.* 14:36, 1926.



the dislocated hip. In each case the position of instability was present due to the development of contractures of the stronger unopposed flexor and adductor muscle groups.

The disturbance of the normal muscle function in group 3, congenital spastic paralysis, was essentially a result of loss of normal muscle coordination, the stronger flexor, adductor and internal rotator groups of muscles forcing the hip joint into the position of instability with resulting dislocation.



Fig. 10 (case 17).—Note reduction of the femoral head in acetabulum. Dislocation and reduction can be accomplished with ease by manipulation without anesthesia.

#### DIAGNOSIS

The clinical signs and symptoms are similar to those present in congenital dislocation. There is a definite limp and lordosis when walking, due to true shortening and posterior displacement of the femoral head in relation to the normal weight bearing line, respectively. A positive Trendelenburg sign may be present due to a disturbance of the integrity of the gluteus medius muscle. Actual and apparent shortening are present on comparative measurements,—the amount of true shortening

in no instance associated with dislocation; the dislocation in the eleven cases was on the side which assumed the attitude of flexion adduction and internal rotation. It is of interest to note the frequency of bilateral involvement of the hip joint in the infectious groups. Figure 15 demonstrates the attitude of flexion abduction and external rotation assumed by the patient at the time of admission to the hospital with an acute septic arthritis of the right hip. One notes that the normal extremity was held in a position of flexion adduction and internal rotation—an instinctive effort on the part of the patient to support and splint



Fig. 9 (case 17).—Residual paralyses of anterior poliomyelitis involving muscles of the right hip joint with resulting spontaneous dislocation.

the involved extremity for the purpose of relieving muscle spasm and pain. The patient complained of pain in both hip joints. The added strain to the normal hip may have caused its lowered resistance, permitting the infection to localize in the joint, with a resulting bilateral infection of the hip joint with one hip in the position of stability and the opposite hip in the position of instability, thus favoring dislocation. It is clear that the muscle spasm should be relieved by means of skin traction and not by support offered by the patient's normal extremity.

The group of patients with residual paralyses of anterior poliomyelitis presented a derangement of the action of the muscles controlling

the ilium. The presence of signs of infection, muscle spasm, muscle paralyses and muscle incoordination depends entirely on the primary etiologic factor.

#### DIFFERENTIAL DIAGNOSIS

The diagnosis of the dislocation as a rule is not difficult, although one may be confused by certain observations. Patient A. R., with residual paralyses of anterior poliomyelitis, with involvement of the hip muscles, presented an habitual posterior and upward dislocation of the



Fig. 12.—Photograph of patient in case 25, figure 11. Note the shortening of the left dislocated extremity held in the position of instability.

femoral head with contractures of the flexor and adductor muscle groups. The onset of anterior poliomyelitis occurred when the patient was 10 years of age, and the mother said that the child had limped since the period of infancy. The dislocation was undoubtedly congenital. Patient F. R. entered the clinic at the age of 14 years with the same clinical signs (fig. 16). The onset of the infantile paralysis was before the patient had started to walk. It could not be stated definitely whether the dislocation was congenital or acquired. Patient S. R. was unable to walk because of the development of a marked flexion adduction and

depending on the degree of displacement upward and the period of time that the stimulus of normal function has been lost. The involved extremity is held in an attitude of flexion adduction and internal rotation with limitation of the opposite movements. There is an abnormal depression of Scarpa's triangle with the head of the femur displaced posteriorly out of the acetabulum. The greater trochanter is above Nelaton's line due to the upward displacement of the femoral head. Telescoping of the



Fig. 11 (case 25).—Polyarticular arthritis, "Still's disease," with spontaneous dislocation of left hip. Note the position of instability of the dislocated hip and the position of stability of the opposite nondislocated hip.

femoral head on manipulation with the pelvis fixed entirely depends on the local pathologic condition. With relaxation of the capsule and absence of fibrosis, there may be marked telescoping; however, the head of the femur may be absolutely fixed due to a fibrous or bony ankylosis of the femoral head to the ilium. The head of the femur is displaced posteriorly and may be palpated in the gluteal region on the dorsum of

There was true shortening, and the greater trochanter was above Nelaton's line. Palpation of bony landmarks was not possible because of the inflammatory reaction. The roentgenogram revealed a fracture of the neck of the femur without dislocation.

#### TREATMENT

I believe that spontaneous dislocation of the hip joint may be considered a preventable condition, and emphasis should be placed on the preventive treatment, because when the deformity is once established, any attempt at correction requires a long period of hospitalization, and



Fig. 14 (patient H. P.).—Note that the correction of the position of instability by skin traction prevented dislocation of the femoral head from the acetabulum.

treatment does not always offer satisfactory correction of the disability. An appreciation of the mechanism of the development of the dislocation should enable one to apply the necessary mechanical apparatus preventing the patient from assuming the position of instability, which is responsible for the dislocation. During the acute stage of any infectious process involving the hip joint, the muscle spasm may be relieved by the application of skin traction and the extremity placed in extension and abduction, which is the position of stability. This method not only relieves muscle spasm and guards against dislocation, but also prevents the patient from utilizing the normal extremity for instinctive traction,

internal rotation deformity of the right hip. Examination revealed residual paralyses of anterior poliomyelitis involving the muscles controlling the hip joint. The head of the femur was easily palpated in the gluteal region; however, a roentgenogram demonstrated that the femoral head was not dislocated. In this instance, the femoral head was easily palpated posteriorly because of the marked atrophy of the gluteus maximus muscle. Patient S. R. entered the clinic with a suppurative arthritis of the left hip with the involved extremity in the position of instability (fig. 18). There was true shortening, and the greater



Fig. 13 (patient H. P.).—Postoperative osteomyelitis of the ischium and greater trochanter. The position of instability resulted from muscle spasm. Note the threatening dislocation of the femoral head from the acetabulum. Dislocation was prevented by the application of skin traction with the extremity in position of abduction and extension. See figure 14.

trochanter was above Nelaton's line. A roentgenogram revealed that the femoral head had not been dislocated from the acetabulum, but a separation of the upper femoral epiphysis with a posterior and upward displacement of the femoral neck had occurred. A woman, G. B., developed a suppurative arthritis of the hip joint following parturition (fig. 17). The involved extremity was held in the position of instability.

than the opposing groups, then apparatus is necessary to maintain the extremity in the position of stability, preventing the development of contractures of the stronger groups of muscles.

Congenital spastic paralysis, as a rule, offers numerous difficulties in treatment. Considerable progress may be made if one is treating a child with fair mentality and cooperative parents. Exercises for the purpose of improving coordination of muscle groups and the prevention of contractures must be employed as early as possible. If the attitude of instability threatens to develop, definite improvement



Fig. 16 (patient F. R.).—Posterior and upward dislocation of the right femoral head. The onset of anterior poliomyelitis occurred before the patient began walking. The differential diagnosis between congenital and spontaneous dislocation is not possible.

often results following a correction of the contractures and obturator neurectomy.

The treatment of patients with an established deformity offers a complicated problem with each case. Frequently the dislocation is a minor lesion, as compared with the associated deformities involving other joints. This is especially true in the paralyses, in which spinal curvature and deformities of the knees and feet may be present, demanding correction before any attention is directed toward reduction of the dislocation.

which places the uninvolved hip in the position of instability and favors bilateral involvement of the hip joint. Following the relief of muscle spasm, the skin traction may be continued for the purpose of partial immobilization of the hip joint, if motion is desired. If one anticipates bony ankylosis, a solid plaster hip spica may be applied in the optimum position for ankylosis to be neutral as regards abduction and adduction and neutral as to rotation and the position of flexion entirely dependent on the occupation of the individual. In children, the hip joint is placed in about 20 degrees flexion.

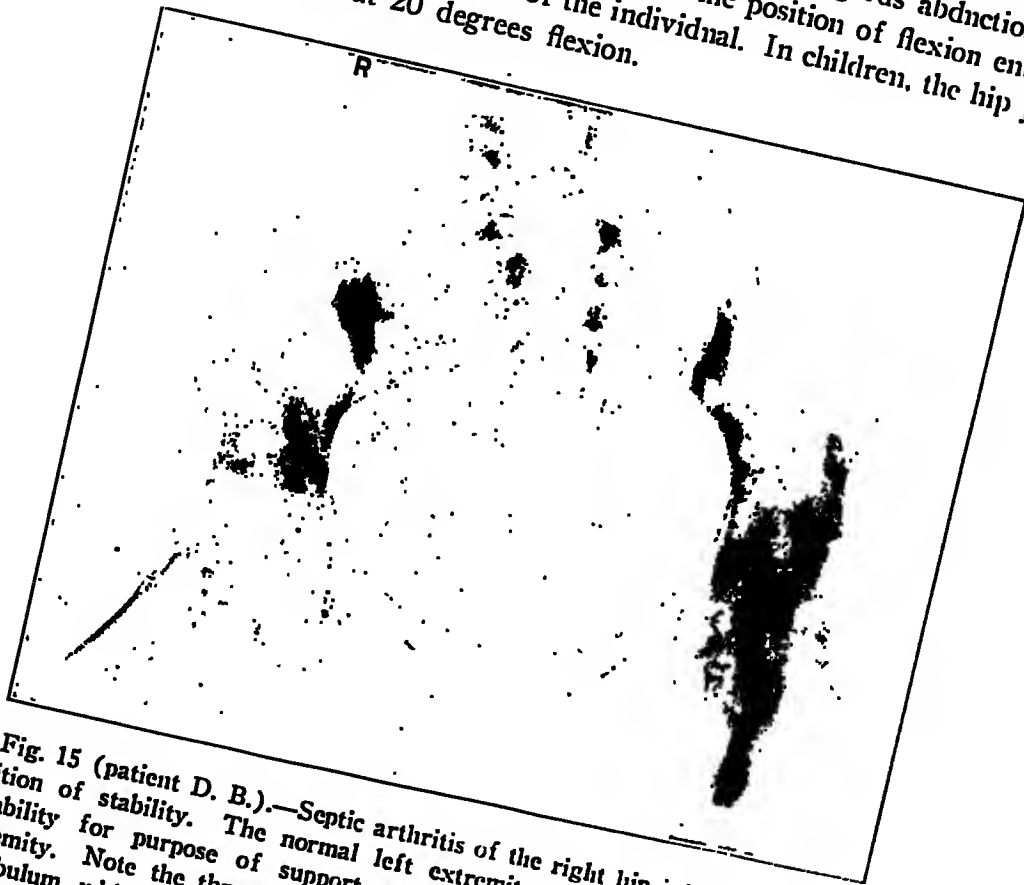


Fig. 15 (patient D. B.).—Septic arthritis of the right hip joint with the hip in position of stability. The normal left extremity was held in the position of instability for purpose of support and instinctive traction of involved right extremity. Note the threatening dislocation of the left femoral head from the acetabulum, which was corrected by application of skin traction to both extremities, relieving muscle spasm and pain.

During the acute tender stage of anterior poliomyelitis with involvement of the lower extremities, the position of stability may be maintained by proper apparatus. With the disappearance of the muscle tenderness, an analysis of the function in which the extremity is to be hip joint will determine the position in which the extremity is to be immobilized, while an attempt is being made for restoration of muscle function. If the adductor and flexor groups of muscles are stronger



and painless hip joint in a good position for weight bearing may be obtained by preliminary skeletal traction, correcting the shortening and pulling the femoral head opposite the acetabulum, followed by arthrodesis of the joint. Two patients of group 1 were definitely improved by this procedure. Fibrous or bony ankylosis between the femoral head and the ilium must be eliminated preliminary to skeletal traction in order to bring the femoral head opposite the acetabulum. In the presence of a bony ankylosis between the femoral head and ilium, a subtrochanteric osteotomy may improve the weight-bearing line and correct the apparent shortening. An attempt to correct the factors



Fig. 18 (patient S. R.).—Purulent arthritis of the left hip with epiphyseal separation; note the position of instability. With obliteration of bony landmarks, due to inflammatory reaction, it would be difficult to rule out posterior dislocation of the femoral head from the acetabulum.

producing disability and to obtain motion is definitely indicated when an ankylosis exists in the opposite hip joint. Preliminary skeletal traction followed by manipulation in an attempt to reduce the femoral head in the acetabulum may be indicated when there has been slight if any bone and joint destruction.

The Lorenz<sup>5</sup> bifurcation operation for the purpose of improving stability and correcting the weight-bearing line was not performed in

5. Lorenz, A.: *New York M. J.* 117:130, 1923.

The treatment of a patient with a dislocation resulting from disturbance of muscle arrangement due to muscle spasm, if seen early, offers a fair prognosis for a functional hip joint. Incision and drainage of abscesses is done, if necessary, and skin traction is applied to the dislocated extremity. The traction is first applied in the line of deformity, and, with the gradual disappearance of muscle spasm, the line of traction is changed by degrees to a position of extension and abduction. Complete reduction was accomplished in two cases by this method, and the patients at the present time, several weeks after reduc-



Fig. 17 (patient G. B.).—Postpartum septic arthritis of the right hip joint; the hip is in a position of instability with pathologic fracture of the femoral neck. It would be difficult to rule out posterior dislocation of the femoral head from the acetabulum in the presence of inflammatory reaction with obliteration of bony landmarks.

tion, are free from active infection and muscle spasm, with a fair range of active hip joint motion.

The degree of disability depends on several important factors: disturbance of weight bearing line; true and apparent shortening; bone and joint destruction; mobility; stability; unilateral or bilateral involvement of the hip joint; associated deformities, and pain.

Stability and mobility are both important factors in the function of the hip joint, stability being the more important. A stable

TABLE 3.—Analysis of Twenty-Eight Cases

Sex	Age at Onset of Disease	Date and Age of Original Admission	Date of Admission for Treatment of Dislocation	Etiology: Septic Arthritis Secondary to	Hip Involved	Attitude of Dislocated Hip Before Treatment	X-Ray Report	Culture and Pathologic Reports	Treatment	Present Condition
M	10 yr.	3/ 0/20 12 yr.	5/ 0/20	Acute rheumatic fever	Left	Flexion adduction, internal rotation	Left hip: no bony destructive changes; upward and posterior dislocation of the head of the femur	Chronic productive inflammation	Preliminary skeletal traction; arthrodesis of left hip	Bony ankylosis of the left hip, in good position for weight bearing
M	0 yr.	4/27/20 6 yr.	4/27/20	Scarlet fever	Bilateral dislocation	Flexion adduction, internal rotation	Bilateral posterior and upward dislocation of the heads of femora; no gross bony destructive changes	Chronic pyogenic infection; no tubercles	Preliminary skeletal traction, followed by manipulation under anesthesia (left hip)	Bony ankylosis of the right dislocated hip, in good position for weight bearing; partial reposi-tion of the left femoral head in acetabulum with fair motion
M	3 yr.	10/ 4/20 4 yr.	10/ 4/20	"Influenza"	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur with formation of secondary acetabulum; no gross bony destructive changes	.....	Preliminary skeletal traction followed by manipulation of left hip under anesthesia	Partial reposi-tion of left femoral head in acetabulum with improvement in weight-bearing line
F	3 yr.	2/10/23 3 yr.	2/10/23	Cervical adenitis and suppurative axillary adenitis	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur; questionable early destructive changes of acetabulum, and femoral neck	.....	Adhesive skin traction, gradually obtaining abduction, and extension	Left femoral head reduced in acetabulum; abducted position maintained at present by plaster hip splint
F	6 yr.	10/23, 27 0 yr.	10/25/27	Tonsillectomy (aspiration pneumonia)	Bilateral dislocation	Flexion adduction, internal rotation	Bilateral destructive lesions involving the head, neck and upper shaft of femora with bilateral posterior and upward dislocation of the heads of femora and bilateral epiphyseal separation	Chronic purulent osteomyelitis; Staphylococcus aureus	Bilateral arthrotomy; bilateral saucerization of femoral shafts; bilateral excision of lateral epiphyses of upper femoral epiphyses	Bilateral discharging sinuses; physiologic position of extremities maintained at present by adhesive traction
F	9 yr.	9/ 7/25 9 yr.	9/ 7/25	"Influenza"	Bilateral; right hip dislocated	Flexion adduction, internal rotation	Destructive process involving both femoral heads and acetabular cavities with posterior and upward dislocation of the head of the right femur	Chronic productive inflammation; no tubercles	Preliminary skeletal traction, and right obturator nerve block followed by open reduction of the right hip	Head of right femur reduced in acetabulum with fibrous ankylosis; attitude of flexion and adduction tends to recur
F	3 yr.	3/21/28 3 yr.	3/21/28	Otitis media	Left	Flexion abduction, external rotation	Left femur: posterior and upward dislocation of the head of the femur; there are beginning bony changes in the head of the femur and acetabulum	Streptococcus hemolyticus	Incision and drainage of abscess of left hip joint followed by adhesive traction	Left femoral head partially reduced in acetabulum; abducted position maintained at present by skin traction

any case reported in this paper. Transplantation of the origin of the tensor fascia lata muscle posteriorly, after the method of Dickson,<sup>6</sup> to improve the stability of the hip joint, was done in two cases in group 2. The stability was appreciably improved in one case.

Mr. H. A. T. Fairbank<sup>7</sup> states that "careful selection of cases suitable for operation is necessary, as in many the extent and severity of the paralysis contraindicate any attempt being made to stabilize the joint."

The dislocation resulting from muscle incoordination in congenital spastic paralysis, as a rule, is not difficult to reduce following preliminary correction of muscle contractures and obturator neurectomy; from my experience, the resulting improvement in function may be entirely disappointing. Continued efforts of the surgeon and of the physiotherapist over a period of many months may not result in any improvement of muscle coordination, on which the ultimate result depends. Unlimited patience and enthusiasm are important factors in dealing with this group of patients.

Improving the stability of the joint by means of forming a new acetabular roof by turning down a bone flap from the side of the ilium, as suggested by Dickson<sup>8</sup> and Jones,<sup>9</sup> was not attempted in this group of patients.

Reefing of the capsule, as performed by Sir Robert Jones,<sup>10</sup> was also not attempted. R. Watson Jones states that, "altho such a procedure may possibly augment the stability of the joint, it cannot supplant the necessity for the prevention of unbalanced muscular action, for, as has been insisted, contractile muscle is stronger than elastic ligament."

Deformities of the knees, feet and joints of the upper extremities are frequently combined with the dislocation of the hip joint in poly-articular arthritis or Still's disease. In one patient of group 4, associated deformities of the opposite hip, knees and feet were improved, following which the dislocation was partially reduced by means of preliminary skeletal traction and manipulation, gaining a definite improvement of function.

Preliminary skeletal traction, followed by manipulation with a satisfactory reduction of the femoral head in the acetabulum, was accomplished in two patients in whom a positive diagnosis of tuberculosis of the hip joint was made. One does not encourage this procedure in the presence of tuberculous arthritis. The positive diagnosis in either case was made subsequent to the foregoing treatment.

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6. Dickson, F. D.: *J. Bone & Joint Surg.* 9:1, 1927.

7. Fairbank, H. A. T.: *Proc. Roy. Soc. Med. (Sec. Orth.)* 16:15, 1923.

8. Dickson, F.: *J. Bone & Joint Surg.* 6:262, 1924.

9. Jones, E.: *J. Orthop. Surg.* 2:183, 1920.

10. Jones, Sir R., and Lovett, R.: *Orthopedic Surgery*, New York: Weller, Wood & Company, 1924, p. 464.

TABLE 3.—Analysis of Twenty-Eight Cases—Continued

Age at Onset of Disease	Date and Age of Original Admission	Date of Admission for Treatment of Dislocation	Etiology: Septic Arthritis Secondary to "Influenza"	Hip Involved	Attitude of Dislocated Hip Before Treatment	X-Ray Report	Culture and Pathologic Reports	Treatment	Present Condition
M	3 yr.	4/10/28	55 yr.	Bilateral dislocation	Flexion adduction, internal rotation	Bilateral destructive process of both hip joints with bilateral posterior and upward dislocation with ankylosis	Staphylococcus aureus	Incision and drainage of abscess	Bilateral bony ankylosis of hip joints; marked disability in gait; ambulatory without crutches
M	2 yr.	4/28/28	22 yr.	Right	Flexion adduction, internal rotation	Right hip: posterior and upward dislocation; complete destruction of femoral head; changes of femoral neck and acetabulum due to abnormal weight bearing	.....	Treatment not advised	Patient is ambulatory with lift on shoe partially compensating for shortening; motion is painless; hip joint is hypermobile; there is 4½ inches shortening
F	10 mo.	5/13/25	6 yr.	Right	Flexion adduction, internal rotation	Paralysis of Anterior Poliomyelitis Right hip: posterior and upward dislocation; no bony changes	.....	Tensor fascia lata transplant	Stability of hip joint not improved by tensor fascia lata transplant
F	3 yr.	11/22/20	13 yr.	Right	Flexion adduction, internal rotation	Right hip: posterior and upward dislocation of the head of the femur; no bony changes	.....	Treatment refused	Fair gait with brace applied; slight instability of right hip
M	2 yr.	5/11/26	5 yr.	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur; no bony changes	.....	Tensor fascia lata transplant	Stability of the hip joint improved following tensor fascia lata transplant
M	10 mo.	8/7/26	22 mo.	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur; no bony changes	.....	Braces applied; extensive paralysis of both lower extremities	Walks with long braces and crutches

6 yr.	11/24/27	27 yr.	.....	Acute osteomyelitis of left tibia	Right	Flexion adduction, internal rotation	Right hip: posterior and upward dislocation of the femur; the head of the femur is not apparent; the neck of the femur and acetabulum show changes in development mainly due to non-weight bearing	.....	No treatment	Patient walks with fair gait; right hip is fairly stable with fair motion; the shortening due to the dislocation is compensated by shortening of the left tibia and fibula, primarily involved with osteomyelitis	Patient walks with fair gait; right hip is fairly stable with fair motion; the shortening due to the dislocation is compensated by shortening of the left tibia and fibula, primarily involved with osteomyelitis
M	10 yr.	21/5/27	17 yr.	Osteo myelitis	Right	Flexion adduction, internal rotation	Right hip: destructive lesion involving the acetabulum, head and neck of the femur; posterior and upward dislocation of the head of the femur with formation of a secondary acetabulum	.....	Preliminary skeletal traction; arthrodesis of the right hip	Bony ankylosis of the right hip in good position for weight bearing	Bony ankylosis of the right hip in good position for weight bearing
M	11 yr.	5/15/21	11 yr.	Infection of the upper respiratory tract	Bilateral; left hip dislocated	Flexion adduction, internal rotation	Destructive lesion involving the femoral head and outer portion of the roof of the acetabulum on the right side; on the left side are multiple areas of destruction involving the neck of the femur and outer portion of the shaft just distal to the greater trochanter		Streptococcus hemolyticus	Subtrochanteric osteotomy of the right femur	Postoperative death due to pyemia
M	11 yr.	11/1/21	15 yr.	Osteomyelitis of the pelvis	Bilateral; right hip dislocated	Flexion adduction, internal rotation	Left hip: marked destructive lesion involving the head and neck of the femur and the entire left ilium; right hip: destructive bony lesion involving the acetabulum, head, neck and trochanter of the right femur with posterior and upward dislocation		Staphylococcus aureus; chronic purulent osteomyelitis	Incision and drainage of multiple abscesses	Death following chronic suppuration
M	23 yr.	7/2/23	29 yr.	Pneumonia	Left	Flexion adduction, internal rotation	Left hip: marked destructive process involving the entire left hip joint and bones surrounding the acetabulum, with posterior and upward dislocation of the head of the left femur		Chronic pyogenic infection; diptheric abscess; empyema culture	Preliminary skeletal traction; arthrodesis of the left hip	Operative death; autopsy report: thrombophlegmasia
M	17 yr.	9/1/21	19 yr.	Acute osteomyelitis of the left clavicle	Left	Flexion adduction, internal rotation	Left hip: bony destructive process involving the head and neck and acetabulum with resulting ankylosis; posterior and upward dislocation of the head of the femur		Staphylococcus aureus	Subtrochanteric osteotomy of the left femur	Improved weight-bearing after following osteotomy
M	14 yr.	7/14/21	11 yr.	"Influenza"	Bilateral; right hip dislocated; left epiphysis atrophic	Flexion adduction, internal rotation	Bilateral destructive process involving both hip joints; posterior and upward dislocation of the head of the right femur; on the left side there is an epiphyseal separation with posterior and upward displacement of the femoral neck		Staphylococcus aureus; chronic purulent osteomyelitis; multiple tubercles	Open resection of the right femoral head in acetabulum	Bony ankylosis of the left hip in near position for weight bearing; recent open reduction wound infected

## CONCLUSIONS

1. Spontaneous dislocation of the hip joint is a preventable deformity.
2. The mechanism of the development of the dislocation is a disturbance of the normal action of the muscles surrounding the hip joint, first emphasized by R. Watson Jones.
3. The disturbance of muscle action may be caused by (a) paralyzes of anterior poliomyelitis with the development of contractures, (b) muscle spasm associated with an infectious process of the hip joint and (c) muscle incoordination of congenital spastic paralysis.
4. Flexion, adduction and internal rotation of the hip should be considered a dangerous attitude.
5. Spontaneous dislocation of the hip joint is essentially a condition developing during early life.
6. Treatment of a patient with an established deformity is highly unsatisfactory, and frequently the dislocation is a minor deformity compared to associated deformities of other joints.
7. Muscle spasm, which is the disturbing factor during the acute stage of infectious arthritis of the hip joint, should be relieved by skin traction maintaining the involved extremity in the position of stability—abduction and extension.
8. Bilateral involvement of the hip joint is frequent in the infectious group.
9. Instinctive traction and support by the normal extremity should be prevented, since it places the uninvolved hip in the position of instability and favors bilateral involvement of the hip joint.

# **Congenital Spastic Paralysis**

1	F	Birth	9 mo 27	23 yr.	Congenital spastic paralysis	Right	Flexion adduction, internal rotation	Right hip: posterior and upward dislocation of the head of the femur with marked changes in the acetabulum, head and neck of the femur due to nonweight bearing	.....	Bilateral obturator neurotomy for painful adductor spasm	Pain relieved following obturator neurotomy
2	F	Birth	2/21/25	9 yr.	Congenital spastic paralysis	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur with no bony changes	.....	Bilateral obturator neurotomy; manipulation under anesthesia	Femoral head reduced in acetabulum but gait not improved
3	F	Birth	1/11/27	1 yr.	Congenital spastic paralysis	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur with no bony changes	.....	Bilateral obturator neurotomy; adhesive skin traction and manipulation under anesthesia	Reduction of femoral head in acetabulum by manipulation under anesthesia failed; second manipulation to be attempted
4	F	Birth	1/19/24	7 yr	Congenital spastic paralysis	Left	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur with no bony changes	.....	Bilateral obturator neurotomy followed by preliminary skin traction and manipulation under anesthesia	Femoral head reduced in acetabulum by manipulation under anesthesia; position maintained at present in plaster hip splint

# **Chronic Polyarticular Arthritis "Still's Disease"**

1	F	4 yr	1 to 27	11 yr	Chronic polyarticular arthritis "Still's disease"	Bilateral; left hip dislocated	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur with atrophic bony changes; right hip: destructive changes involving the femoral head and acetabulum with a loss in joint space	.....	Weighting plasters correcting flexion deformities of the knees and hips	Flexion deformities practically corrected; patient is gradually becoming ambulatory after a period of 6 years remissionary
2	F	1 to 27	1/11/25	7 yr.	Chronic polyarticular arthritis "Still's disease"	Bilateral; left hip dislocated	Flexion adduction, internal rotation	Left hip: posterior and upward dislocation of the head of the femur with atrophic changes of the head and neck of the femur; right hip: destructive lesion involving the femoral head and acetabular cavity	.....	Weighting plasters correcting flexion deformities of the knees and hips, followed by skeletal traction and manipulation under anesthesia	Ambulatory without braces; gait is fair; patient had been recumbent for a period of 6 years

# **Tuberculous Arthritis**

1	M	10	9/1/0	33	Tuberculous arthritis	Bilateral; left hip dislocated	Flexion adduction, internal rotation	Right hip: destructive lesion without bone regeneration involving the femoral head, neck and acetabulum; left hip: posterior and upward dislocation with no destructive changes	Tuberculous report; positive evidence of tuberculous	Prothylary skeletal traction; manipulation under anesthesia; motion discontinued on girdle-splint report	Recumbent with both hips immobilized in physiologic position; complete reduction of left hip in acetabulum
2	F	10	9/10/0	6 yr	Tuberculous arthritis	Bilateral; left hip dislocated	Flexion adduction, internal rotation	Right hip: destructive process involving the neck, femoral head and acetabulum without bone regeneration; left hip: posterior and upward dislocation with a destructive lesion involving the head of the femur and acetabulum	Girdle-splint report; positive evidence of tuberculous	Prothylary skeletal traction; manipulation under anesthesia	Death following chronic suppuration





Fig. 1.—Stomach of dog 7 with jejunal transplant. Note acute ulcer of pyloric mucosa with gastritis and erosions of fundal mucosa.

# EFFECT OF INJECTIONS OF HYDROCHLORIC ACID ON THE GASTRIC AND DUODENAL MUCOSAE\*

WILLIAM J. GALLAGHER, M.D.

CHICAGO

In a previous communication,<sup>1</sup> it was shown that acute traumatic lesions of jejunal transplants to the stomach healed readily in the presence of artificial hyperacidity. I shall now report the changes observed in the gastric and duodenal mucosae of those experiments and further observations in a group of control animals fed acid solution.

## EXPERIMENTAL PROCEDURE AND RESULTS

The experimental procedure was described in a previous report.

Briefly, after recovery from the intestinal transplant operation, a group of seven animals were fed acid solution through a stomach tube once or twice daily in amounts of from 200 to 225 cc. and in concentrations of 0.22, 0.29 and 0.62 per cent by weight.

A group of six control dogs was similarly studied, into which 0.62 per cent acid solution was injected two or three times daily. The injections were given daily from ten to eighty days. On various occasions, the contents of the stomach of several of the dogs were aspirated from four to five hours after the injections of acid. The animals were kept on a diet of meat, bones, bread and water. After daily injections had been given for about one month, there was considerable loss of weight, but emaciation did not occur in any of the dogs. Acidosis was observed in several, most of which were then killed. Immediately after the death of the dogs, specimens were excised for microscopic examination and placed in Zenker's fluid to prevent postmortem changes.

In the group of seven animals in which jejunal transplants had been made, vomiting was frequent, especially with the higher concentration of acid solution. From 8 to 30 cc. of contents was obtained at different times on aspiration five hours after injection, while in the control experiments, the stomachs were always empty after five hours.

Mucus was frequently present in the vomitus and was constantly present in the stomachs. Blood stained mucus and tarry stools were observed in two dogs.

The changes in the mucosa of the stomach were more extensive with the higher concentration of acid solution and the more frequent injections.

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\* From the Seymour Coman Fellowship in the Department of Physiology of the University of Chicago and the Department of Surgery of Pritzker Medical College of the University of Chicago.

1. Gallagher, W. J.: *Arch. Surg.* 17:279 (Apr.) 1922.

especially in the experiments with jejunal transplant in which there was often some delay in the emptying time of the stomach.

The most marked changes were always observed in the fundal mucosa. Briefly, these were acute and chronic gastritis with superficial and deep erosions and acute ulcers in a few animals; in one, a chronic ulcer, 3 by 1.5 cm., was located on the middle of the anterior wall. This dog had been fed 0.62 per cent acid solution from one to two times daily for fifty-nine days. A jejunal transplant was also on the anterior wall,

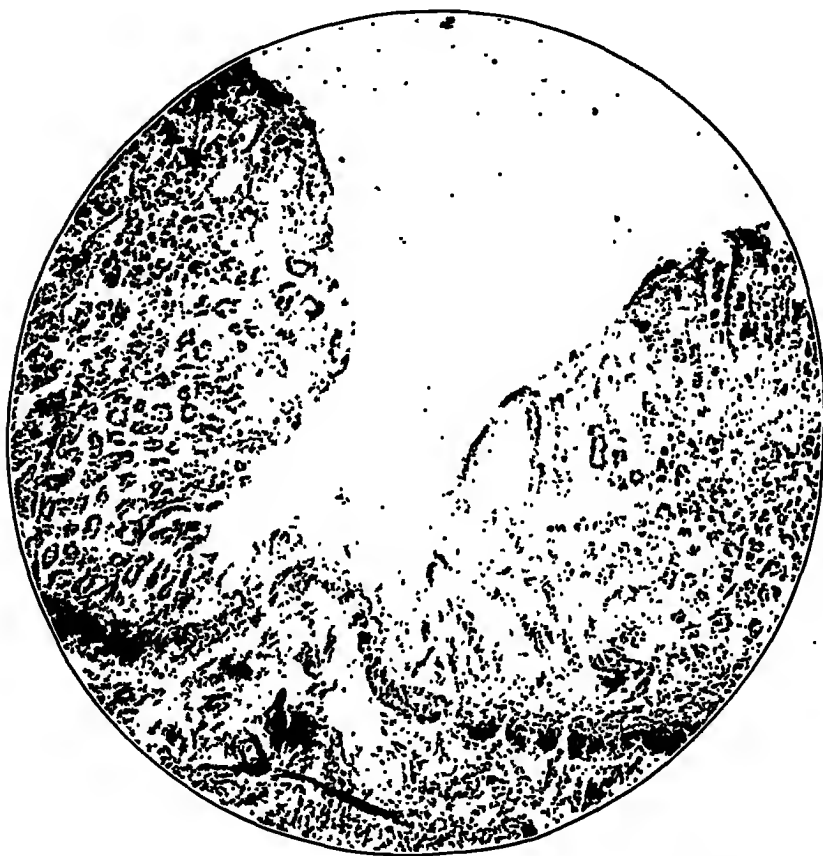


Fig. 4.—Deep erosion of fundal mucosa in figure 1. Note slight cellular exudate;  $\times 50$ .

but was not in any way connected with the chronic ulcer. The base of the ulcer was formed by submucosa which contained considerable scar tissue; there was little change in the muscularis, and there was only slight cellular infiltration about the ulcer. In three animals, acute erosions were present in the pyloric mucosa. Two of these were in the group of control animals. Two acute ulcers, 5 by 3 mm. were observed in the pyloric mucosa near the lesser curvature in one dog fed 0.62 per cent acid twice daily for twenty-five days.



Fig. 2.—Acute ulcer in figure 1. Note cellular infiltration of mucosa and submucosa;  $\times 50$ .



TABLE 1.—*Effect of Injections of Hydrochloric Acid on Gastric and Duodenal Mucosae\**

Dog	Injections of Hydrochloric Acid			Necropsy	
	Per-centage	Amount of Each Injection, Cc.	Number of Days	Results	Histologic Studies
1	0.22	200	33	Stomach dilated, contains mucus; congestion and swelling of gastric mucous membrane; a few superficial erosions in fundus	
2	0.20	200	50	Congestion, swelling, petechial hemorrhages and superficial erosions 1 to 2 mm. in size; mucus present; area of redness, 1 cm. in size, on posterior wall of duodenum near pylorus	Superficial and deep erosions with some cellular infiltration of gastric mucosa; some cellular infiltration of duodenal mucosa
3	0.22 0.62	200 200 twice daily	53 20	Blood stained mucus in stomach; many erosions in fundus, a few in antrum, 1 to 3 mm. in size; two acute ulcers in fundus 2 by 1 cm.; first 4 cm. of duodenal mucosa on posterior wall are reddened and contain two erosions 1 to 2 mm. in size; tarry material in colon; edema and redness generally of gastric mucosa	Acute ulcers extend into submucosa; cellular infiltration of submucosa, with eosinophils and round cells; a few fibroblasts at base of ulcers; cellular infiltration of mucosa in many areas; deep and superficial erosions
4	0.22	200	32	Some mucus in stomach; edema and redness but no gross erosions of gastric mucosa	
5	0.62	200	60	Mucus in stomach; edema and redness of gastric mucosa with superficial erosions in fundus, 1 to 2 mm. in size	Eosinophils and round cells in mucosa and submucosa; exudate in mucosa; superficial and deep erosions present
6	0.62 0.62	200 225 twice daily	27 32	Much mucus in stomach; edema, petechiae and several erosions of fundal mucosa, 1 to 2 mm. in size; chronic ulcer of the gastric mucosa, 3 by 1.5 cm., on anterior wall middle of fundus; hard, gray base; mucosa puckered about ulcer	Much exudate on surface of mucosa which contains superficial and deep erosions and marked cellular infiltration in duodenum; scar tissue in base of chronic ulcer for 2 mm. beneath mucosa on either side of ulcer; base formed by submucosa; little cellular infiltration of ulcer
7	0.62 0.62	200 200 twice daily	19 6	Much mucus in stomach; edema, redness, many erosions of gastric mucosa, the largest 1 cm. in diameter; two acute ulcers near lesser curvature of pylorus, 5 by 3 mm.; 2 cm. of posterior wall of duodenum are reddened	Superficial and deep erosions with round cells and eosinophils in mucosa of stomach; much exudate with round cells, eosinophils in duodenal mucosa

\* These animals had jejunal transplants to the stomach for from 41 to 151 days. There was some tendency to retention and more frequent vomiting after acid injection than in the control dogs fed neld solution.



Four of the controls did not show gross change or only slight thickening of the pyloric mucosa. Mucus was usually found in this region in large quantities.

A localized duodenitis with superficial erosions was observed near the pylorus and usually on the posterior wall in four of the seven experiments in which jejunal transplants were made, and in five of the six controls. In three, gross erosions were present in the area of redness in the duodenum.



Fig. 8.—Fundal mucosa showing marked cellular infiltration of mucosa and submucosa;  $\times 50$ .

Histologic studies were made in most of the experiments. Sections were taken from various parts of the gastric mucosa and from the inflamed areas of the duodenal mucosa.

In many areas of the fundal and duodenal mucosae, cellular infiltration was marked. In the acute regions, exudate with polymorphonuclear leukocytes was observed. In the more chronic lesions, round cells, plasma cells and eosinophils were present.



Fig. 6.—Chronic ulcer in figure 5. Note the scar tissue in base and the proliferative single layer of cells at the margin:  $\times 50$ .



Fig. 7.—Reactive cross reaction in ulcer margin. Note the cellular reaction:  $\times 80$ .



The erosions were superficial and deep, some extending to the submucosa. In some erosions, cellular infiltration was slight; in others, it was marked and in places extended into the submucosa. The lesions extending into the submucosa were termed ulcers. Where the erosions

TABLE 2.—*A Series of Injections of Hydrochloric Acid Into Stomach of Normal Dogs\**

Dog	Injections of Hydrochloric Acid			Necropsy	
	Per- cent- age	Amount of Each Injec- tion, Cc.	Number of Days	Results	Histologic Studies
1	0.62	225 two to three times daily	80	Tarry material in colon; blood stained mucus in stomach; edema, redness, many erosions of fundal mucosa 1 to 2 mm. in size, also an acute ulcer, 8 by 8 mm.; petechiae, redness of mucosa of duodenum for 6 cm. from pylorus	Exudate and cellular infiltration of gastric mucosa with superficial and deep erosions; cellular infiltration and exudate of duodenal mucosa, many lymph follicles in mucosa of duodenum
2	0.62	225 twice daily	31	Edema and redness of fundal mucosa; much mucus in stomach; pyloric mucosa normal grossly; edema and redness of duodenal mucosa for 6 cm. from pylorus	
3	0.62	200 three times daily	10	Mucus in stomach; a few erosions of pyloric mucosa 1 mm. in size; edema and redness of fundal mucosa on posterior wall of duodenum is an erosion 8 by 1 mm. which is surrounded by redness for 1 to 2 cm. and 0.5 cm. from pylorus	Superficial and deep erosions of gastric and duodenal mucosa, 1 to 2 mm. in size, with cellular infiltration and exudation
4	0.62	200 twice daily	29	Mucus in stomach; edema, redness and many erosions of gastric mucosa, 1 to 10 mm. in size; erosions 1 to 2 mm. in size near lesser curvature of pylorus; redness for 5 cm. and a few erosions 1 mm. in size on the posterior wall of duodenum	Superficial and deep erosions of gastric and duodenal mucosa; some cellular infiltration
5	0.62	200 twice daily	41	Redness and swelling of fundal mucosa with several erosions 1 to 2 mm. in size	Exudate, cellular infiltration, superficial and deep erosions of gastric mucosa, also of duodenal mucosa
6	0.62	200 twice daily	36	Mucus present in stomach; edema, redness and erosions of fundal mucosa 1 to 2 mm. in size with similar changes in the first 1 to 2 cm. of the posterior wall of the duodenum	Superficial and deep erosions with cellular infiltration of the gastric and duodenal mucosa; some exudate on the surface

\* Acidosis frequently developed after which the animal was usually killed.

were superficial, exudate was usually limited to the mucosa, and in many areas exudate poured from the eroded tubules.

In the pyloric and duodenal mucosae, these inflammatory changes were usually localized, while in the fundal mucosa they were frequently diffuse.

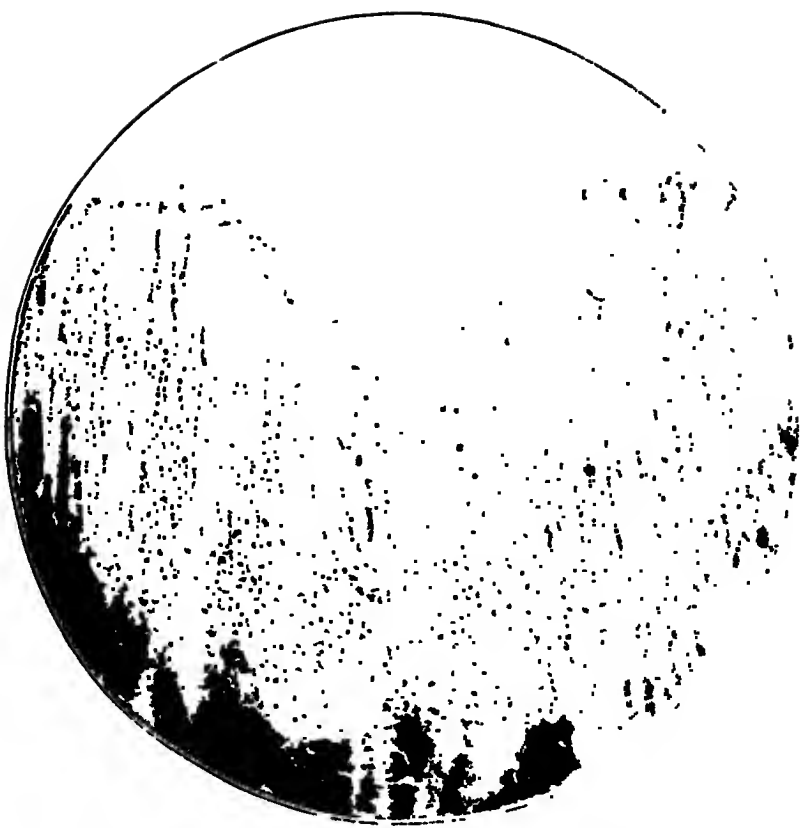


Fig. 9.—Stomach of control dog 5 showing a superficial erosion of the mucosa with only slight cellular infiltration;  $\times 50$ .



irritating acid solution with the mucosa. The more frequent vomiting in these animals, however, lessened the time of contact to some extent. Gravitation of mucus to the pylorus with regurgitation of alkaline intestinal contents and the alkaline secretion of the pyloric mucosa, no doubt, explain the few changes observed in the pyloric mucosa.

The location of the chronic gastric ulcer suggests the possibility that repeated trauma from the stomach tube and the forceful flow of acid



Fig. 12.—Control dog 4, showing superficial erosion of duodenal mucosa with marked cellular infiltration. Note Brunner's glands with two lymph follicles beneath exudate;  $\times 50$ .

solution from the tube produced an acute lesion which was daily traumatized by these factors. Trauma and acid solution were important in the production of this lesion.

The localized duodenitis, usually close to the pylorus, is further evidence of the irritating action of hydrochloric acid. The changes in the duodenum were never observed more than from 2 to 6 cm. distal to the pylorus. This suggests the possibility of neutralization of the acid beyond these areas. The gross and microscopic appearance of these

## COMMENT

Bolton<sup>2</sup> observed similar changes in the stomachs of cats and monkeys, but he used much higher concentrations of acid solution.

Carlson<sup>3</sup> and recently Palmer<sup>4</sup> have found 0.5 per cent of hydrochloric acid in the analysis of gastric secretions of normal dogs; 0.62 per cent is higher than normally found. However, the changes produced in animals given 0.22 and 0.29 per cent acid differed only in degree



Experimentally at least, hydrochloric acid is an important element in the production of acute and chronic gastritis with erosions and acute ulcers.

#### SUMMARY

The changes produced by injecting different concentrations of hydrochloric acid into the stomachs of thirteen dogs have been studied. The experiments were carried out on two groups. In one group of seven animals with jejunal transplants to the stomach, acid was injected once or twice daily in amounts of from 200 to 225 cc. of a 0.22, 0.29 or 0.62 per cent solution. Vomiting was frequent; mucus was present in the stomachs in large quantities. There was frequently some delay in the emptying time of the stomach in these animals. The greatest changes were usually present in the fundal mucosa. Acute ulcers were observed in the pyloric mucosa of two animals, while a chronic gastric ulcer of the fundal mucosa was observed in one. Repeated trauma from the stomach tube was suggested as a factor in the production of this lesion. The most constant observations were acute and chronic gastritis with multiple erosions; these changes were greater when the higher concentrations of acid were used. A localized area of duodenitis, with erosions in two, was present in four of the seven animals.

In the second group of six control animals, a 0.62 per cent solution was injected in similar amounts two or three times daily. Chronic ulcers were not observed, but changes similar to those in the stomachs and duodenal mucosae of the animals in the first group were noted, although to a lesser degree. A delay in the emptying time of the stomachs of this group was not observed.

Histologic studies were made of different parts of the gastric and duodenal mucosae showing different types of erosions, acute ulcers and cellular changes.

Attention is called to the similarity of these lesions to those found clinically in the stomach and duodenum and the probable importance of hydrochloric acid in their production.

#### CONCLUSIONS

1. Acute and chronic gastritis and duodenitis with multiple erosions and acute ulcers are produced by injections of hydrochloric acid into the stomachs of dogs.

2. A delay in the emptying time of the stomach causes more extensive changes of the mucosa of the stomach, and when an element of trauma is added, a chronic ulcer may occur.

3. Mucus may exert a protective influence against the corrosive action of hydrochloric acid on the gastric mucosa.

duodenal lesions are strikingly similar to those occurring in the human being to whom an average of 63 units of free hydrochloric acid has been given (Judd and Nagel).<sup>5</sup>

The gastric lesions are also grossly and microscopically similar to those described by Orator,<sup>6</sup> Konjetzny<sup>7</sup> and others in the stomachs of persons with ulcer.



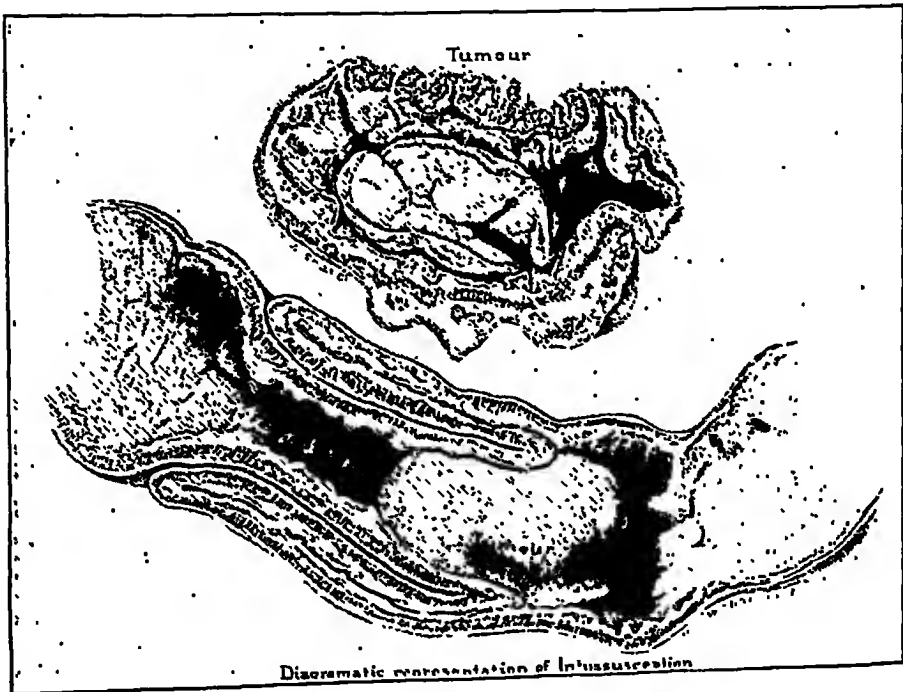
Fig. 13.—Gastric mucosa of control dog 4, 57 minutes after ingestion of 100 cc. of 10% HCl. Note engorgement of vessels in submucosa;  $\times 150$ .

made a fairly rapid recovery and left the hospital in three weeks with a fistula at the site of the operation. She returned to the hospital two months later and the fistula was closed.

She was seen again in January, 1928, with an attack of obstruction of the small bowel, and was admitted to the hospital. An operation disclosed that the obstruction was due to a band. This was relieved, and the patient left the hospital in eighteen days. She has been well since that time.

#### COMMENT

Submucous lipomas of the colon are comparatively rare. The most comprehensive study found in the literature was that by P. DeRocque and A. DeRocque,<sup>1</sup> who made a study of all the cases reported up to



Lipoma of the colon with diagram of intussusception.

1924, numbering 104. Approximately the same number were found in the small bowel as in the colon; 34 per cent of the cases in the small intestine and 9 per cent of those in the large intestine were symptomless. In thirty-one cases, an emergency operation was performed for acute obstruction. In fifty-six cases, the patient suffered from chronic obstruction. In forty-seven of these cases, intussusception occurred, this phenomenon being more common in the small intestine than in the colon. The DeRocques suggested that the most suitable treatment is an enterotomy and enucleation of the tumor, but that in some cases in which the diagnosis is doubtful, a resection should be undertaken.

1. DeRocque, P., and DeRocque, A.: *J. de chir.* 24:163 (Aug.) 1924.





# CANCER OF THE LOWER LIP

SUGGESTIONS AS TO OPERATIVE TECHNIC IN PLASTIC REPAIR \*

FRED R. FAIRCHILD, M.D.

WOODLAND, CALIF.

The motive for the presentation of this subject is to describe an operation for the reconstruction of the lip. As the necessity for the procedure arises almost wholly from cancer, the characteristics of the disease must first be considered, at least so far as they exert a modifying influence on operative technic.

In view of the claims of many competent observers that better results are obtained by radiation than by operation in the treatment of cancer of the lip, one almost feels the necessity of arguing the point to establish his right to suggest a surgical procedure. To do this would be but to add another personal opinion to one side of an argument that only further experience and the lapse of time can settle. No better illustration of the radical difference of opinion relative to the method of choice could be had than that offered by the symposium on intra-oral cancer presented before the Radiological Society of North America in November, 1926. Papers read by Ewing<sup>1</sup> of New York, Burnham<sup>2</sup> of Baltimore, Duffy<sup>3</sup> of New York, and Judd and New<sup>4</sup> of Rochester served to give the conviction that no one is certain whether irradiation or operation offers the best chance of cure. Until the question is answered, a cancer of the lip should be treated as an entity, and, after careful consideration of all modifying conditions, experience must be the guide in determining whether radiation or a surgical procedure should be used.

There cannot be any question that the poor cosmetic effect following resection of cancer of the lip is a factor that influences many patients to select treatment by radiation, even in the face of an analysis of the situation resulting in positive advice that surgical intervention would be the safer procedure. The patient will often accept an added percentage of risk to escape disfigurement. The surgeon will sometimes allow his heart to rule his head. These factors often cause the patient to insist on a conservative course; this may or may not be regrettable, if he consults a competent radiologist, but the result will surely be most unfortunate if, as so often happens, he falls into the hands of a quack.

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\* From the Department of Surgery, Woodland Clinic.

\* Read at the Meeting of the Pacific Coast Surgical Association held in Portland, Ore., Feb. 22-25, 1928.

1. Ewing, James: *Radiology* 9:359 (Nov.) 1927.

2. Burnham, C. F.: *Radiology* 9:366 (Nov.) 1927.

3. Duffy, J. F.: *Radiology* 9:373 (Nov.) 1927.

4. Judd, Starr, and New, G. B.: *Radiology* 9:380 (Nov.) 1927.



growths were cancer, and microscopically, they were cancer, but there was not any way of knowing what the behavior of the individual tumor would be.

Not until 1920, was any material progress made in the ability to estimate the degree of malignancy in any cancerous growth. At this time,

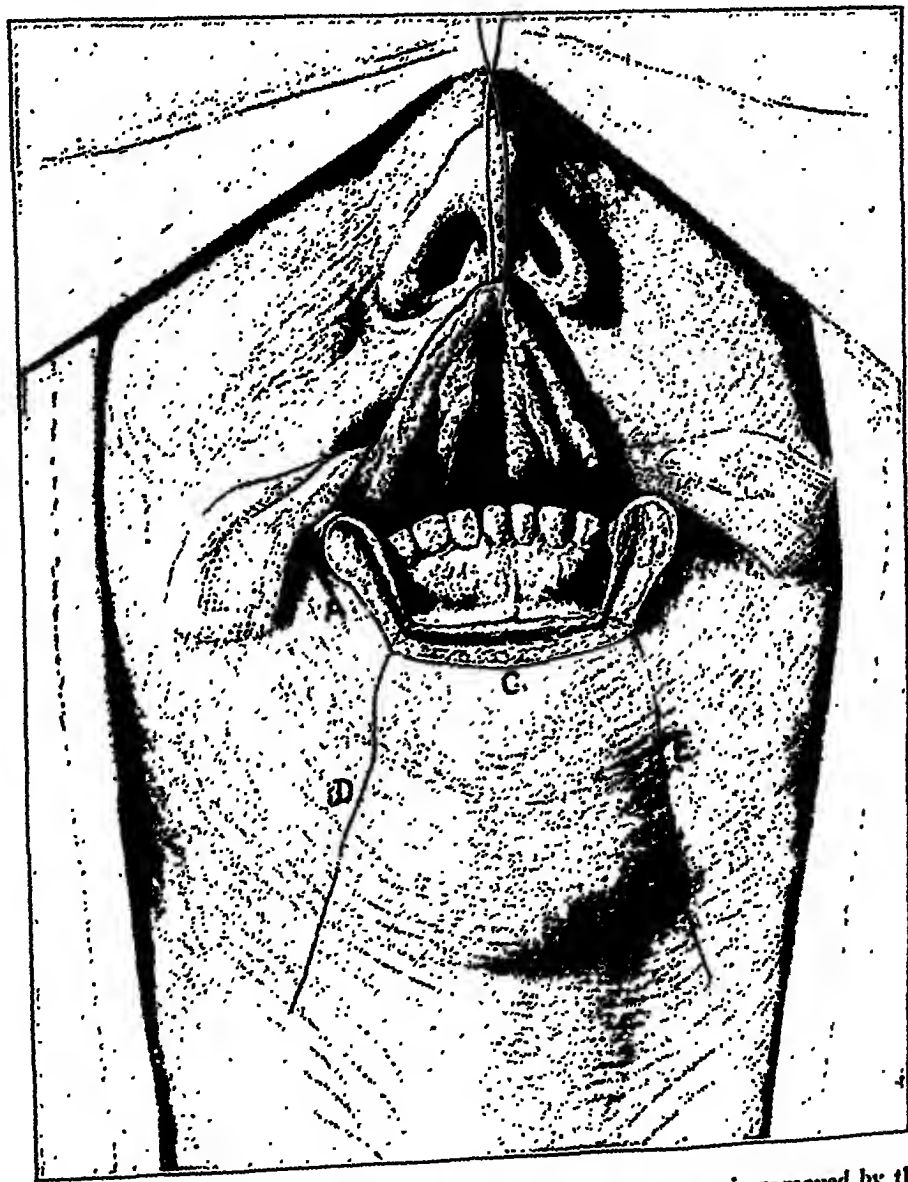


Fig. 2.—First step in the operative procedure. The tumor is removed by three incisions through the entire thickness of the lip. *A* and *B* are vertical incisions on either side of the tumor; *C*, the transverse incision connecting the lower extremities *A* and *B*. In the second step, *D* and *E* indicate the obliquely vertical skin and fat incisions made to mobilize the flap for tissue to form the body for the new lip.

Broders studied a series of cancers of the lip from the immense amount of material at his disposal. His conclusions were that those tumors, the cells of which showed the greatest tendency to differentiation and



surgeons hesitate to venture a prognosis as to the outcome of even the most innocent appearing cancerous lesion until its grade is known. A knowledge of the grade of malignancy of a cancer puts one in possession of the most important fact in the determination of whether treatment by surgery or by radiation is the method of choice.

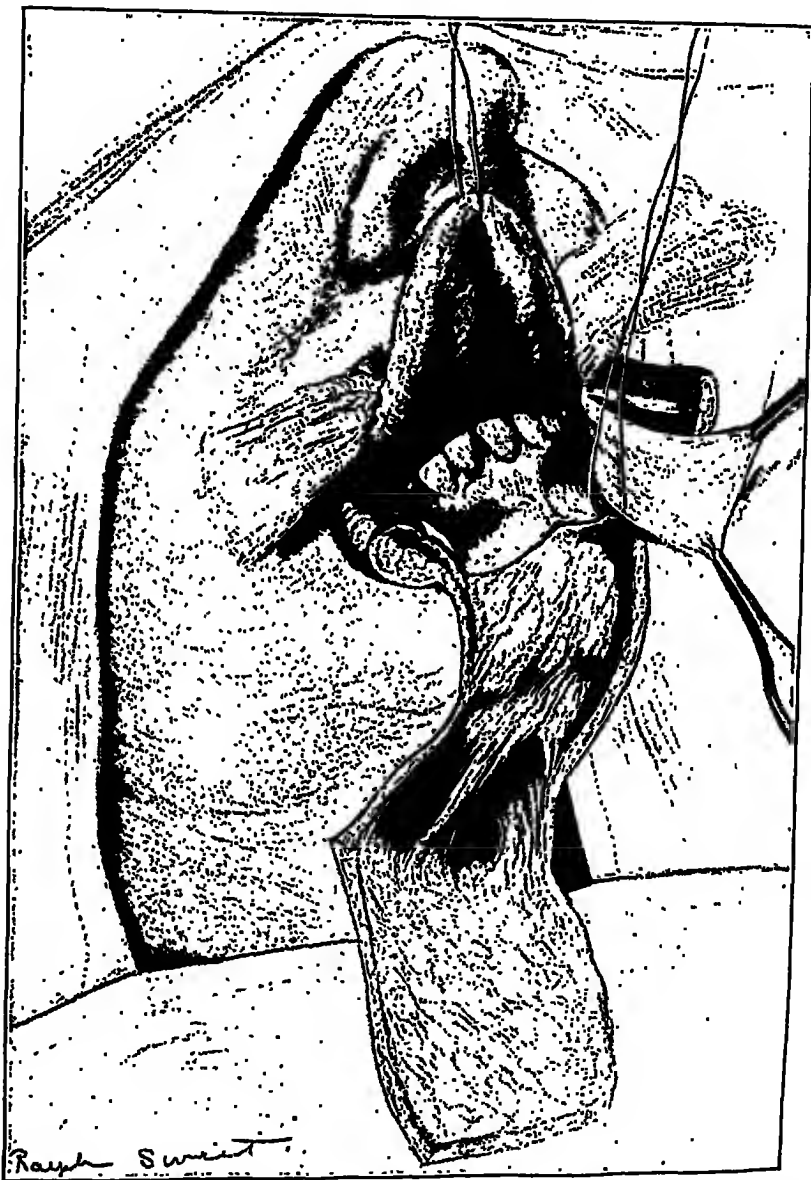


Fig. 4.—Fourth step in the operative procedure showing the method for securing the mucous membrane flaps to cover the buccal portion of the new lip. These flaps must be of sufficient width to permit covering the upper portion of the skin fat flap to form the normal vermilion line.

Judd<sup>4</sup> states that the results obtained at the Mayo Clinic are in accord with the observations of Simmons<sup>5</sup> of Boston, a member of the Cancer Committee appointed by the American College of Surgeons,

5. Simmons, C. C.: *Surg. Gynec. Obst.* 43:377, 1926.

keratinization, were least vicious. These, in grade of malignancy, he classed as I. Those tumors, the cells of which did not tend to differentiate, but did tend to infiltration into the deeper structures, he classified as most malignant and put them in grade IV. Grades II and III, in order of malignancy, were placed between grades I and IV.



Fig. 3.—Third step in the operative procedure. With the submental flap dissected free, sufficient skin and fat tissue is obtained to cover the defect, and this exposure makes possible the unusual cervical lymphatic dissection.

Pathologists and surgeons generally have been slow in accepting this classification as of value. Repeated observations on the postoperative courses of those patients on whom the grade was determined have compelled a rather general acceptance of the value of the grading. Some

approximate accord with my observations at the Woodland Clinic. I have never seen a cancer of grade IV that did not show recurrence within a year no matter how innocent clinically the lesion appeared, how radical had been the surgical extirpation, or how intensive the post-operative radiation. Simmons concludes that "the type of operation

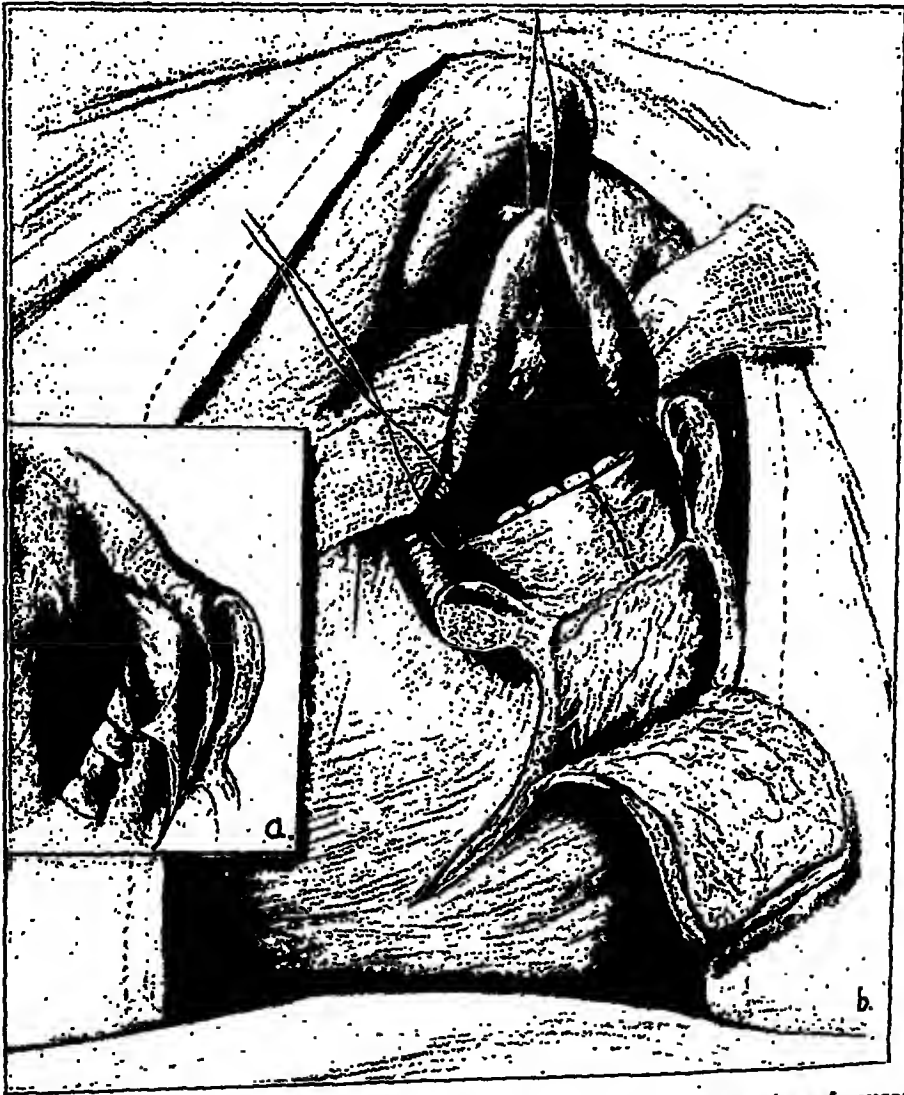


Fig. 6.—Fifth step in operative procedure. Section *b* shows the lateral mucous membrane flaps sutured in a median line and to the mucous membrane edge formed by a transverse incision (*C*, fig. 2). Section *b* illustrates the immediate closure of the buccal mucous membrane defect made in securing the mucous membrane flaps.

performed apparently made little difference. The cases in group I recovered, while those in group IV died."

"Applying these observations to the subject under discussion, I believe that in every case of cancer of the lip, irrespective of the apparent grade

in 1922. The investigations of this committee, considering cancer generally, led to the conclusion that "in primary cases without evidence of metastasis surgical treatment offers a thirty-five per cent chance of permanent cure against fifteen percent by irradiation, while in primary cases in which there are clinical signs of metastasis, radium offers no chance of permanent cure and radical surgery not more than 5 per cent."

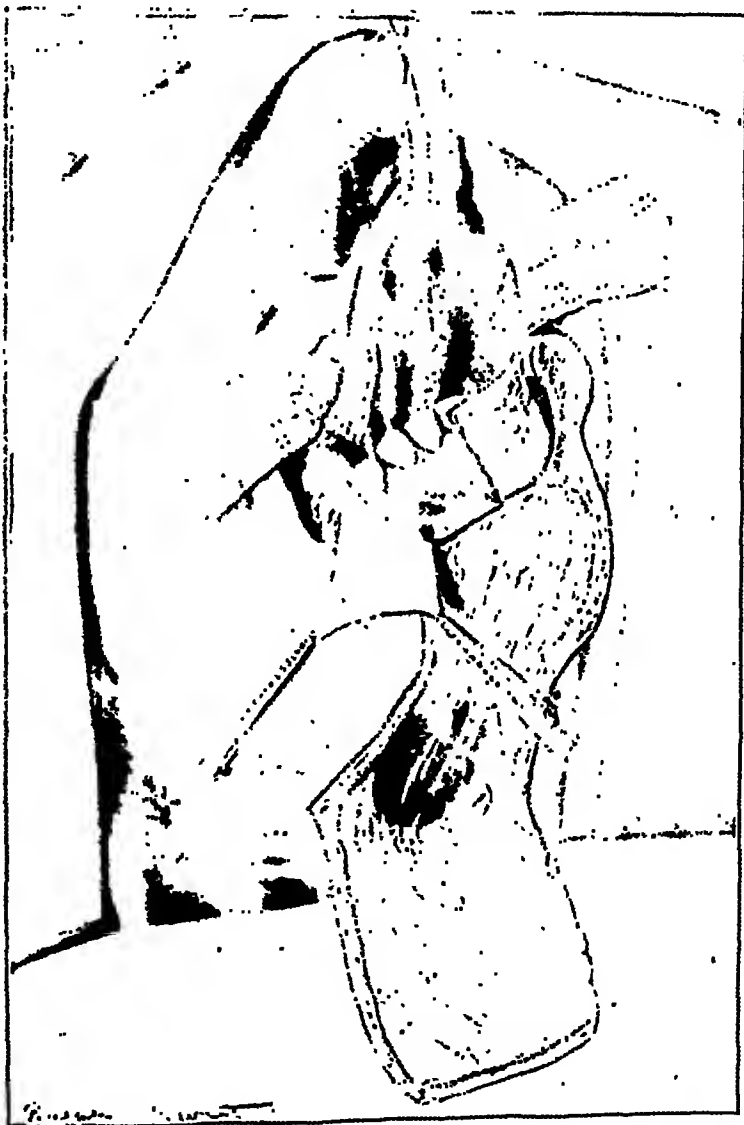


Fig. 5.—Lower border of the left flap sutured in place; the first suture of the right flap in place showing knots on the inside of the flap.

Simmons' report is further of extreme interest in that it bears out the experience of those who have had the good fortune to have all their operative cases graded. He reported that in cancer of grade I, 68 per cent of permanent cures were effected; of grade II, 21 per cent; of grade III, 6 per cent, and of grade IV, none. These conclusions are in



of any surgical technic which will not limit the surgeon in radical extirpation of the tumor and of the distal adjacent lymphatic system, and will at the same time permit him to obtain a better cosmetic effect.

There cannot be an ideal operation for cancer of the lip, for the nature of the lesion compels the sacrifice of all tissue that is under the

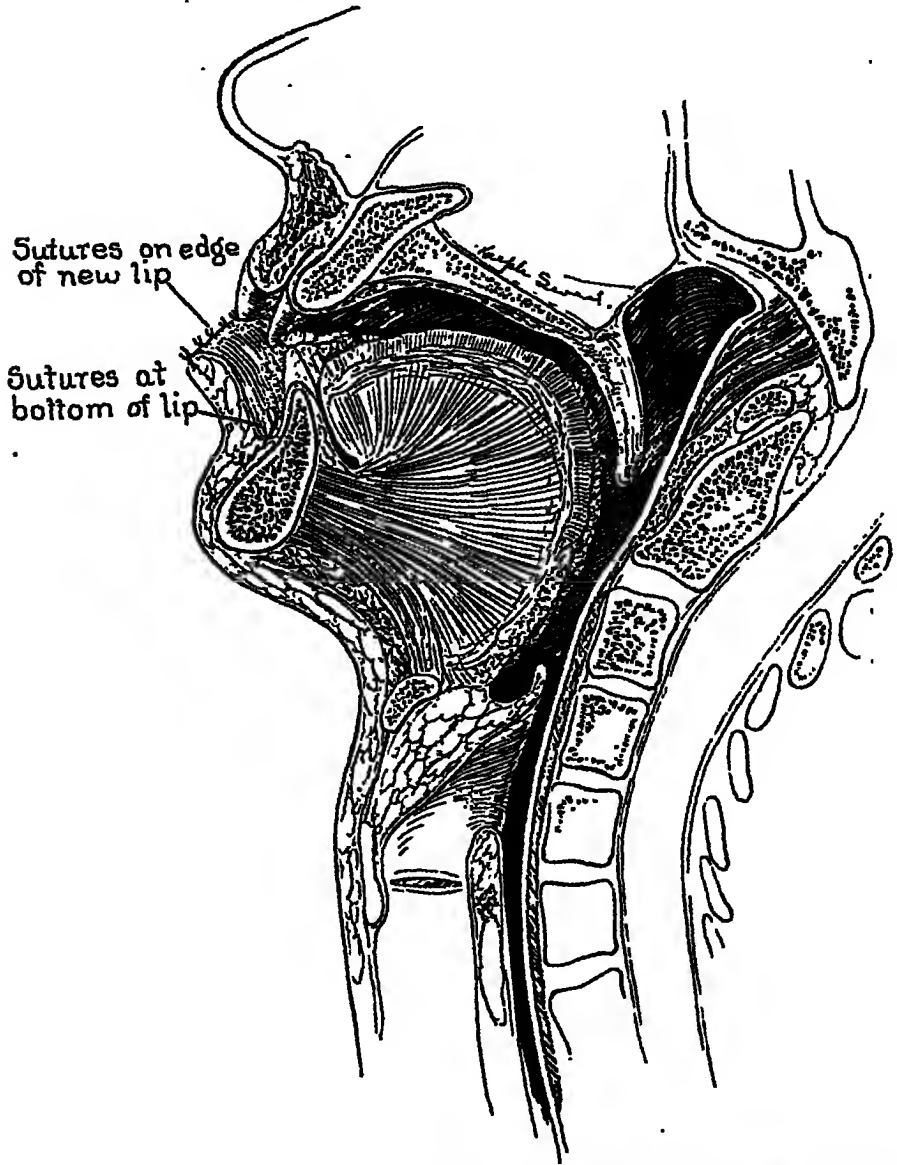


Fig. 8.—Schematic drawing of the sagittal section illustrating the normal sulcus between the reconstructed lip and gums of the lower teeth.

suspicion of involvement. Ewing calls particular attention to the transverse course of the blood and lymph stream in the lips, and emphasizes the relative frequency of local recurrence following the "V"-shaped excision (fig. 1). This circumstance, he believes, may be due to the development of a new tumor by lateral embolism rather than to the

of malignancy, a biopsy should be performed. Surgical intervention should not be performed on any tumor of grade IV, and there is serious question whether it is of value in cancers of grade III if there is positive metastasis. Radiation offers as much relief, and by conservative treatment the patient's short span of life will probably be less distressing.

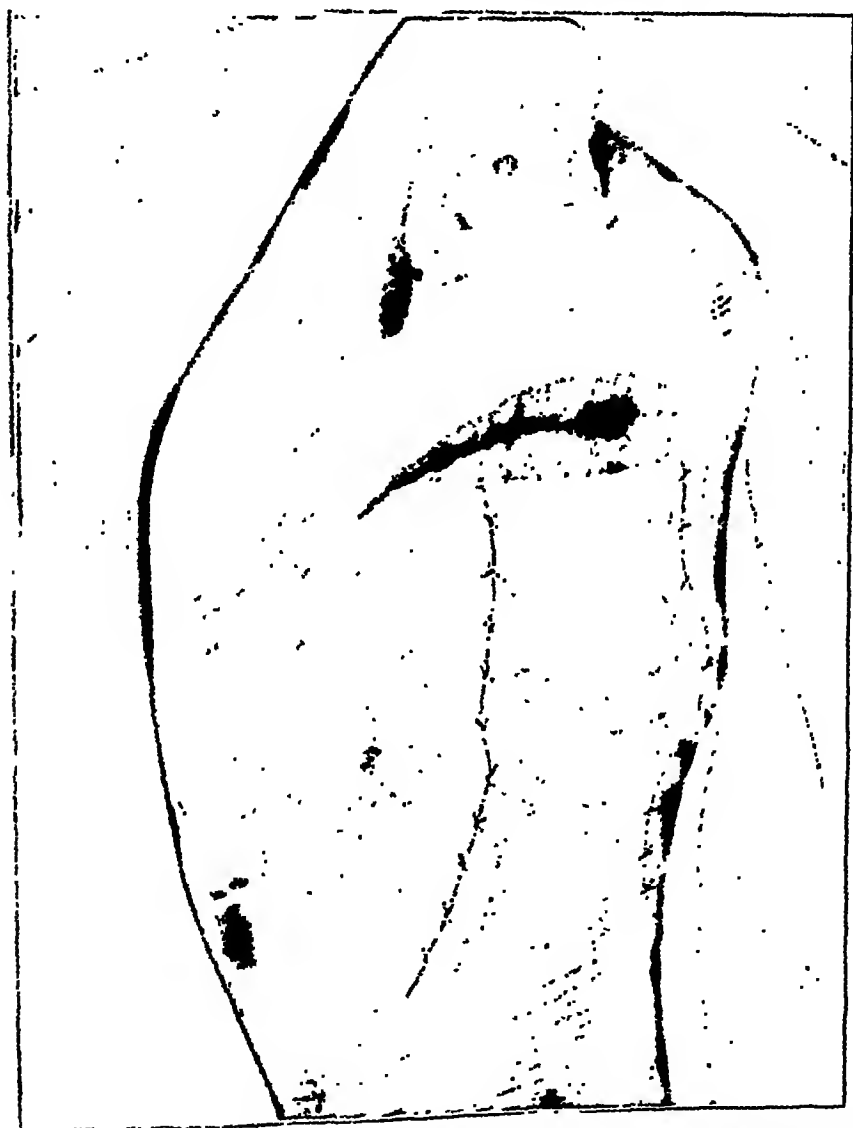


Fig. 7.—Sixth step in the operative procedure showing the skin fat flap suture in place. The buccal mucous membrane flap is sutured to the skin margin, being reflected over the upper border of the skin fat flap to form the labial mucosa and vermillion line.

According to Simmons' statistics, cancers of grades I, II or even III without evidence of metastasis, show a higher percentage of cures by surgical intervention than they do by radiotherapy. As the majority of cancers of the lip fall into these classifications, a discussion is justified

zontal incision with the edge of the mucous membrane below the lower horizontal incision (figs. 5 and 6).

STEP 6.—The skin and fat flap is then sutured in place by dermal sutures, placed obliquely to distribute such tension as may be present along the entire suture line. The upper border of the united mucous membrane flaps is reflected over the upper border of the skin and fat flap and sutured to the skin line with interrupted chromic catgut sutures to form the vermillion line (fig. 7).

The advantages of this method are: 1. There is nothing in the procedure to cause contractures lessening the size of the mouth. 2. There is nothing to interfere with the most radical extirpation of the tumor with that portion of the lymphatic system which is under suspicion. 3. The entire operation can be completed in one stage. 4. The lower lip does not tend to tighten against the teeth, interfering with a plate, if, as so often happens, one has to be worn. 5. The sulcus in front of the lower incisors is of normal depth (fig. 8).

survival of old tumor cells. If his presumption is correct, it is obvious that the patient is in jeopardy from lateral as well as from vertical metastasis, and that any competent surgical procedure must take into account and eliminate this source of probable recurrence as certainly as it does the danger of recurrence from spread through the cervical lymphatic system.

This means that frequently the only chance of obtaining a cure lies in an apparently ruthless sacrifice of the entire lower lip. The ideal surgical procedure would permit this, with a dissection of the gland-bearing fat envelope, and allow for a satisfactory reconstruction at one operation. No reconstruction can be made entirely satisfactory to the patient, for no plastic lip can have the mobility and expression of the original.

I believe, however, that the technic to be described comes nearer to fulfilling the requirements than any other method I have seen.

Credit is not claimed for originality in any part of the procedure. It is merely a composite technic made up of various steps in other operations.

#### OPERATIVE TECHNIC

**STEP 1.**—That portion or all of the lower lip to be sacrificed is excised by three incisions extending through the entire thickness of the lip: a vertical incision on either side of the tumor, with a transverse incision placed at the level of the point of the chin connecting the lower extremities of the vertical incisions (fig. 2).

**STEP 2.**—From the lower angles of the rectangle formed by the foregoing procedure, bilateral incisions are made through skin and fat running downward and slightly outward for a distance of from 2 to 3 inches (5 to 7.6 cm.). When the skin and fat flap between the two incisions is dissected free, it will be found possible to draw the flap up without tension, a sufficient amount to fill in the deficiency caused by the sacrifice of the lower lip (figs. 2 and 3).

**STEP 3.**—The submental area is already exposed. The vertical and obliquely vertical incisions previously made on each side permit easy exposure for completion of the usual lymphatic dissection (fig. 3).

**STEP 4.**—Provision has been made for the skin and fat flap to replace the sacrificed lip. A mucous lining must be supplied for the intra-oral portion of this flap. On each side, such a flap is formed by making two horizontal incisions through the buccal mucosa. The upper incision originates at a point about  $\frac{3}{4}$  inch (0.63 cm.) above the angle of the mouth and extends backward for  $2\frac{1}{2}$  inches (6.27 cm.), passing just below the opening of Stenson's duct. The lower incision is parallel to it and of equal length, and originates at a point corresponding to the lower angle of the excised rectangle. These flaps of mucous membrane are dissected up from before backward. It will be found that the flaps can be pulled to the median without tension (fig. 4).

**STEP 5.**—The extremities of the two mucous membrane flaps are sutured with interrupted, 00 chromic catgut. Similarly, the lower borders of these flaps are sutured to the cut edge of the mucous membrane at the margin of the gum. The denuded area behind the mucous membrane flaps is closed by interrupted chromic catgut sutures, uniting the edge of the mucous membrane above the upper hori-

The third primitive layer of cells, the mesoderm, first appears between the ectodermal and entodermal layers of the embryonic disk. As it proliferates, it insinuates itself peripherally between the entoderm of the yolk-sac and the ectoderm of the enveloping layer. Ultimately, it extends to surround also the ectoderm of the amniotic cavity. By internal cleavage, the peripheral portion of the mesoderm is divided into an outer parietal

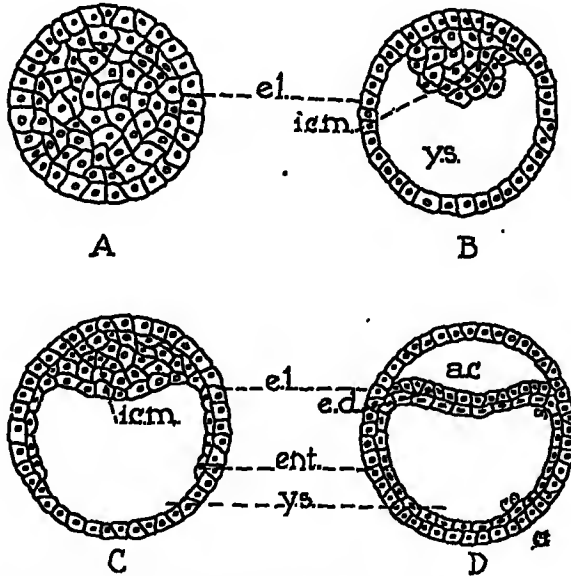


Fig. 1.—A, section of morula with enveloping layer (*e.l.*); B, section of embryo with yolk-sac (*y.s.*) and inner cells mass (*i.c.m.*); C, section of embryo with proliferating entoderm (*ent.*); D, section of embryo with embryonic disk (*e.d.*) and amniotic cavity (*a.c.*) (after Bailey and Miller in Textbook of Embryology).

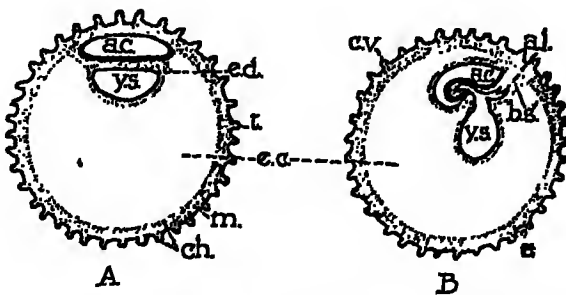


Fig. 2.—A, transverse section of embryo showing relation of mesoderm (*m.*) to embryonic disk (*e.d.*), yolk-sac (*y.s.*), amniotic cavity (*a.c.*), and trophoderm (*t.*), extra-embryonic celom, (*e.c.*), chorion, (*ch.*) (after Bailey and Miller). B, longitudinal section of embryo with body stalk (*b.s.*), allantois (*a.*) and chorionic villi (*c.v.*) (after McMurrich: Development of the Human Body).

layer attached to the interior of the enveloping layer and an inner visceral layer applied to the exterior of the entoderm of the yolk-sac. The space thus formed by the cleavage of the mesoderm is called the extra-embryonic celom. Meanwhile, the enveloping layer becomes dif-

# EXSTROPHY OF THE BLADDER COMPLICATED BY CARCINOMA

E. STARR JUDD, M.D.

AND

HAROLD L. THOMPSON, M.D.

ROCHESTER, MINN.

Carcinoma complicating exstrophy of the bladder is rare; we have noted reports of only nineteen cases in the literature, two of which were reported by Scholl<sup>1</sup> from the Mayo Clinic. We are adding one case (case 1) which has not been reported previously. So far as we know, cure has not been reported following treatment. In two cases at the Mayo Clinic, however, the patients have remained well for three and six and a half years, respectively, following surgical treatment.

## EMBRYOLOGY

It is assumed that the fertilized human embryo, by processes of growth and cell division, soon becomes a solid mass of cells, the morula. The peripheral cells of the morula differentiate and thus form a distinct enveloping layer of cuboidal cells<sup>2</sup> (fig. 1 *A*). Vacuoles which appear within the enclosed mass of cells coalesce to form a single cavity within the enveloping layer. This cavity corresponds to the yolk-sac of certain lower species, and hence that name is retained for it. A small mass of cells attached to the interior of the upper pole of the enveloping layer persists as the inner cell mass (fig. 1 *B*). The cells of this mass that are contiguous with the yolk cavity differentiate and proliferate over the inner surface of the enveloping layer to form a complete lining for the yolk-sac. This layer is called the primitive entoderm (fig. 1 *C*). Meanwhile, vacuoles appear also within the inner cell mass, and these coalesce to form the amniotic cavity. This cavity is enclosed by the enveloping layer (fig. 1 *D*); in the floor of this cavity a layer of cells persists, called the embryonic plate or disk. In addition to enclosing the embryo proper, the enveloping layer forms the wall of the amniotic cavity and the outer layer of the wall of the yolk-sac, and thereby envelopes the entire embryo. At this stage of development the embryo consists essentially of the embryonic disk composed of two layers, a layer of ectodermal cells which occupies the floor of the amniotic cavity, and an approximated layer of entodermal cells which is a part of the lining of the yolk-sac.

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1. Scholl, A. J.: The Potential Malignancy in Exstrophy of the Bladder, *Ann. Surg.* 75:365, 1922.

2. Bailey, F. R., and Miller, A. M.: *Textbook of Embryology*, New York, William Wood and Company, 1923, pp. 84-121.

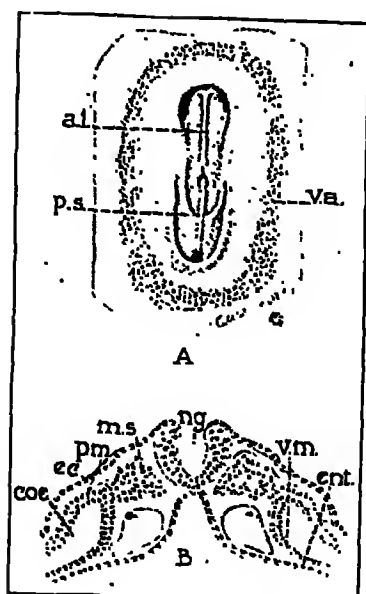


Fig. 3.—*A*, germinal disk with primitive streak (*p.s.*), axillary line (*a.l.*) and *v.a.*, vascular area. *B*, transverse section of germinal disk with neural groove (*n.g.*) and mesoderm between ectoderm (*e.c.*) and entoderm (*ent.*) which is divided by a longitudinal groove into a paramesial solid portion forming the mesodermic somites (*m.s.*) and a peripheral portion which is cleft by the celom (*coe.*) forming parietal mesoderm (*p.m.*) and visceral mesoderm (*v.m.*) (after Bailey and Miller).

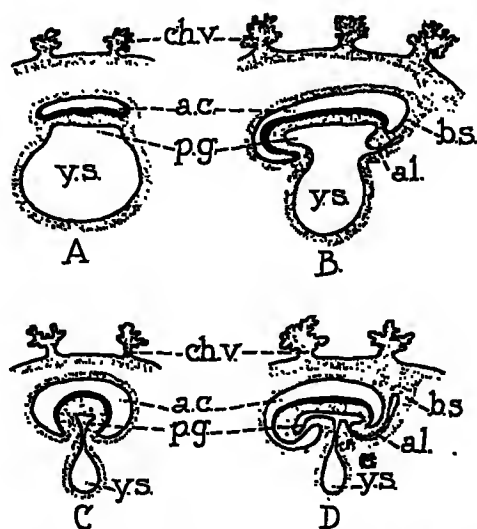


Fig. 4.—Sections of embryo with constriction between embryo and yolk-sac. *A* and *C*, transverse sections; *B* and *D*, longitudinal sections. *ch.v.*, chorionic villi; *a.c.*, amniotic cavity; *p.g.*, primitive gut; *y.s.*, yolk-sac; *al.*, allantois; *b.s.*, body stalk (after McMurrich).

ferentiated into two distinct layers, an outer syncytial and an inner cellular layer, which together comprise the trophoderm, so named from the rôle it plays in the nutrition of the embryo. The trophoderm and the parietal mesoderm together comprise the chorion<sup>2</sup> (fig. 2 *A*). As a result of the enlargement of the extra-embryonic celom, the embryo proper becomes separated increasingly from the chorion and remains attached to it only by a cord of mesoderm known as the body stalk<sup>3</sup> (fig. 2 *B*). The youngest human embryos which have been observed are at this stage of development.

While the formation of the primitive embryonic layers proceeds in this way, a linear opacity, the primitive streak, gradually becomes manifest on the surface of the embryonic disk. Anterior to the primitive streak, an opaque band, the axial line, appears<sup>2</sup> (fig. 3 *A*). In a cross-section of the latter, it is seen to be composed of a local proliferation of cells of all the primitive layers. As mentioned, the proliferating mesoderm insinuates itself between the ectoderm and entoderm, and the peripheral portion undergoes internal cleavage. In sections, the mesoderm is seen to be divided by a shallow longitudinal groove into the peripheral cleft portion and a paramesial solid portion. The surface of the paramesial solid portion of the mesoderm becomes segmented transversely, forming somites or body segments. A longitudinal groove which appears in the ectoderm of the axial line gradually deepens to form the neural groove. By subsequent fusion of the margins over the trough of this groove, the neural tube is formed<sup>2</sup> (fig. 3 *B*).

In its earlier stages, the embryonic disk may be conceived of as floating on the upper portion of the yolk-sac. Subsequently, a furrow develops at the periphery of the disk and deepens progressively until the opposing edges approximate and fuse ventrally in the median plane, thus giving cylindric form to the embryo<sup>3</sup> (fig. 4 *C*). A portion of the yolk-sac is thereby constricted off and enclosed within the embryo as the primitive digestive tract, while by the same process the amniotic cavity is extended completely around the embryo and forms a constriction about the body stalk which thus completes the formation of the umbilical cord. The anterior and posterior extremities of the embryo meanwhile fold ventrally on the body, forming respectively the head and tail folds<sup>3</sup> (fig. 4 *D*). The embryo at this stage is suspended in the amniotic cavity by the umbilical cord.

Early in the history of the yolk-sac, the allantois originates from it as an evagination<sup>4</sup> (fig. 5). Its growth proceeds through the body stalk

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3. McMurrich, J. P.: *Development of the Human Body*, ed. 7, Philadelphia, P. Blakiston's Son & Co., 1923, p. 41.

4. Lewis, F. T.: *The Early Development of the Entodermal Tract and the Formation of its Subdivisions*, in Keibel and Mall: *Manual of Human Embryology*, Philadelphia, J. P. Lippincott Co., 1912, vol. 2, p. 295.



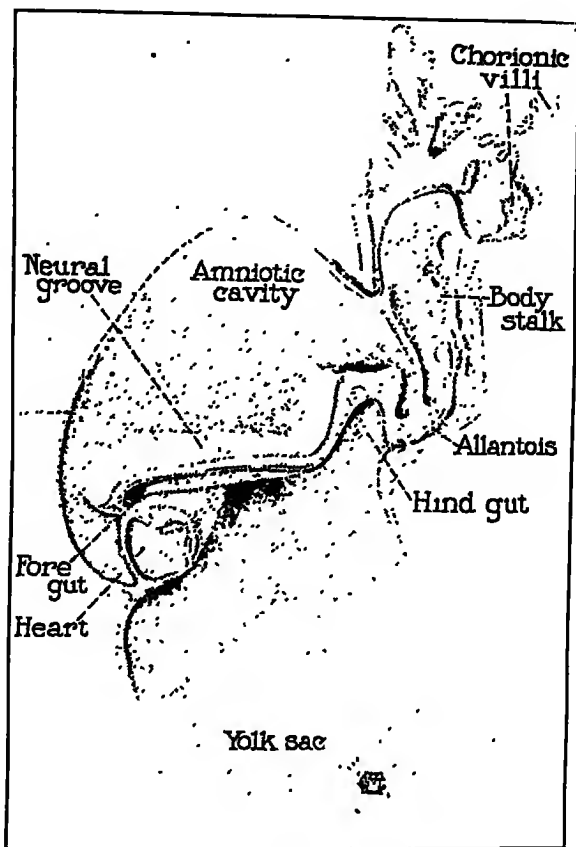


Fig. 6.—Median longitudinal section of Mall's series 391 (after Lewis in Keibel and Mall: Manual of Human Embryology).

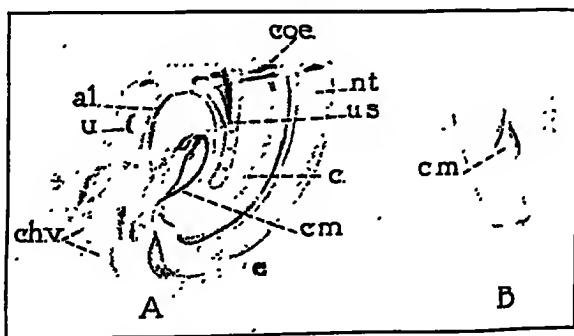


Fig. 7.—A, median longitudinal section of model of caudal region of embryo from His' collection in which gradual separation of the bladder from the rectum is shown diagrammatically by the series of dotted lines (after Keibel and Felix in Keibel and Mall: Manual of Human Embryology); B, ventral aspect of model of caudal region of embryo from His' collection in which cloacal membrane (*c.m.*) occupies the bottom of a groove (after Keibel).

and ultimately reaches the placenta <sup>4</sup> (fig. 6). The foregut and hindgut originate also as evaginations of the yolk-sac. The caudal portion of the hindgut expands as the cloaca, the interior of which communicates directly with that of the hindgut and that of the allantois. In man the cloaca is a temporary structure, but in the amphibia, reptiles and birds it is permanent.

During the formation of the tail-fold, the ventral portion of the cloacal entoderm becomes approximated to and fuses with the ventral ectoderm to form the cloacal membrane <sup>5</sup> (fig. 7 A). Through increase

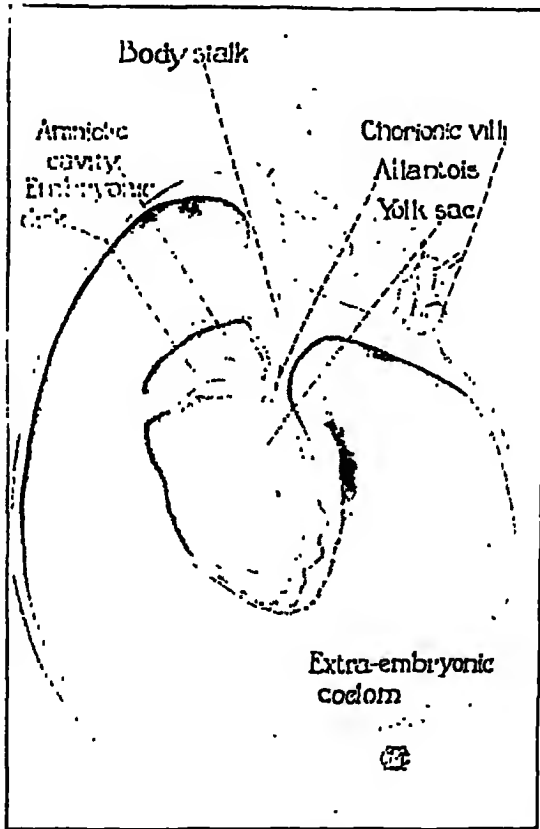


Fig. 5.—Median longitudinal section of Minot's embryo (after Lewis in Keibel and Mall: *Manual of Human Embryology*).

in the surrounding mesoderm, this membrane becomes folded into the substance of the embryo so that seen from without it lies at the bottom of a shallow groove situated at the ventrocaudal region of the body <sup>6</sup> (fig. 7 B).

5. Felix, W.: The Development of the Urinogenital Organs, in Keibel and Mall: *Manual of Human Embryology*, Philadelphia, J. P. Lippincott Co., 1912, vol. 2, p. 869. Keibel, F.: Zur Entwicklungsgeschichte der Harnblase, *Anat. Anz.* 6:186, 1891; Zur Entwicklungsgeschichte des menschlichen Urogenitalapparates, *Arch. f. Anat. u. Entw.*, 1896, p. 55.

6. Footnote 5 (second and third references).

Brunn<sup>10</sup> and Albarran.<sup>11</sup> Bridoux<sup>12</sup> pointed out that while many observers agree on the existence of these glands their descriptions of them are not in accord. It appears, therefore, that the question of the existence of glands in the mucosa of the normally developed bladder remains an open one.

In reported histologic studies of exstrophy of the bladder, on the other hand, glands have been observed consistently. Thus, glandular tissue was present in each of a total of eighteen cases of exstrophy of the bladder examined by Shattock,<sup>13</sup> Enderlen<sup>14</sup> and Scholl.<sup>1</sup> The ages of their patients ranged from a few months to 77 years. In the cases of two new-born infants, on the other hand, Enderlen found normal transitional epithelium but did not find glands, and Formiggini<sup>15</sup> found cystic cavities but did not find glands. Enderlen concluded that glandular tissue normally is present in cases of exstrophy of the bladder in which the patient is more than a few months of age.

The literature on the histogenesis of glandular mucosa in exstrophy of the bladder has been reviewed by Formiggini. Enderlen interpreted its presence as a result of metaplasia following a functional change in the mucosa induced by mechanical irritation, by drying and the decomposition of urine. Ehrich<sup>16</sup> expressed the belief that the glands develop from a displaced or undeveloped spur of cloacal entoderm whereby embryonic epithelium of the dorsal or rectal wall of the cloaca is included in the ventral or vesical wall. Reichel<sup>17</sup> proposed the explanation that the glands result from failure of cloacal epithelium to be differentiated normally as vesicle epithelium and that thus it contains glands like those of the rectal mucosa. Righetti<sup>17</sup> studied histologically the rectum of a patient with exstrophy of the bladder and found that the mucosa of the rectum in certain areas contained epithelium of the vesical type and in other regions undifferentiated epithelium, which he interpreted as evol-

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10. Von Brunn, A.: Ueber drüsenähnliche Bildungen in der Schleimhaut des Nierenbeckens, des Ureters und der Harnblase beim Menschen, *Arch. f. mikr. Anat.* 41:294, 1893.

11. Albarran, J.: *Les tumeurs de la vessie*, Paris, G. Steinheil, 1892, pp. 494.

12. Bridoux, Henri: A Case of Adenoma of the Bladder with Remarks on the Pathology of the Affection, *Am. J. Urol.* 9:514, 1913.

13. Shattock, S. G.: *Specimens of Epispadias and Extroversio Vesicae Showing an Attachment of the Muscular Wall of the Bladder to the Back of the Pubic Bones*, Tr. Path. Soc., London, 1894, vol. 45, p. 117.

14. Enderlen, E.: *Zur Histologie der Schleimhaut der ektopierten Blase*. Verhandl. d. deutsch. path. Gesellsch. 7:167, 1904.

15. Formiggini, Benedetto: Contributo allo studio istologico della mucosa vesicale extrofica, *Riforma med.* 36:252, 1920.

16. Ehrich, E.: Gallertkrebs der ekstrophierten Harnblase, *Beitr. z. klin. Chir.* 30:581, 1901.

17. Quoted by Formiggini.

The primary excretory duct, which is formed by the fusion of the tubules of the pronephros, grows downward and joins the ventral portion of the cloaca. Later, it serves as the excretory duct of the mesonephros, at which time it is known as the wolffian duct. From this, the anlage of the permanent kidney is formed.

Both the bladder and the rectum are formed from the cloaca by the downward extension of the fold of tissue between the allantois and the hindgut. The partition thus formed is known as the urorectal septum<sup>7</sup> (fig. 7-1). The ventral portion of the cloaca thus divided is the vesico-urethral anlage, and the dorsal portion is the rectal anlage. Fusion of the urorectal septum with the cloacal membrane divides the latter into an anterior urogenital and a posterior anal membrane. The cephalad portion of the vesico-urethral anlage retains its attachment to the allantois. The bladder finally is formed by the enlargement and cephalad growth of the vesico-urethral primordium, the caudal portion remaining narrow as the urethra. By gradual absorption of the lower portion of the wolffian duct by the vesico-urethral anlage, the ureter comes to open into it. Gradually, the urethral orifice is shifted to its final position at a point lateral to and above the orifice of the wolffian duct. Meanwhile, the allantois undergoes retrogressive changes by which ultimately it is reduced to a solid fibrous cord which extends from the apex of the bladder to the umbilicus as the urachus. The anal opening is formed by perforation of the anal membrane. Thus it is seen that the bladder and rectum are derived from a common embryonic structure, the cloaca.

### HISTOLOGY

The histologic structure of the bladder in persons with exstrophy usually is unlike that of the normal bladder. The lining epithelium of the normal bladder characteristically is of the transitional type. Statements to the effect that glands in the mucosa of the normal bladder do not exist appear in some authoritative works on anatomy (Piersol<sup>7</sup>) and histology (Bohm, von Davidoff and Huber<sup>8</sup>). In others, it is stated that usually in the mucosa about the urethral orifice and occasionally also in the fundus of the bladder mucous follicles are present which have been described as glands by several observers, including Kölliker,<sup>9</sup> von

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7. Piersol, G. A.: *Human Anatomy*, Philadelphia, J. P. Lippincott & Co., 1923, vol. 2, p. 1909.

8. Bohm, A. A.; von Davidoff, M., and Huber, G. C.: *The Pelvis of the Kidney, Ureter and Bladder*, in *Textbook of Histology*, Philadelphia, W. B. Saunders Co., 1916, p. 337.

9. Kölliker, A.: *Physiological Remarks: Development of the Urinary Organs*, in *Manual of Human Histology*, London, The Sydenham Society, 1854, vol. 2, p. 208.

brane. Von Geldern<sup>22</sup> accepted the view of Johnston<sup>23</sup> that the cause of exstrophy of the bladder complicated by intestinal fistula is early rupture of the cloacal membrane with arrested development of the urorectal septum. He suggested also that disturbance of chemical balance underlies these factors.

Young considered Keibel's theory the most tenable. Keibel demonstrated that the cloacal membrane arises from the caudal portion of the primitive streak, in some cases extending beyond its usual anterior limit on to the body stalk and thereby covering the region which gives rise to the genital papilla and a portion of the lower abdominal wall. He considered the primitive streak of mammals as the equivalent of the blastophore of lower vertebrates and expressed the belief that exstrophy of the bladder results, therefore, from persistent open blastophore.

Gilis agreed with Keibel that exstrophy of the bladder results from the perforation of the cephalad extension of the cloacal membrane, but he did not agree that it has the phylogenetic significance attributed to it by Keibel. Gilis added what seems to be a significant point; that normally the infra-umbilical region is strengthened by the medial growth of the protovertebral laminae of mesoderm which give rise to the abdominal muscles and fascia. Exstrophy of the bladder may result, therefore, from failure of these muscles in their development sufficiently to reinforce the cloacal membrane.

#### PATHOLOGY

Carcinoma is a rare complication of exstrophy of the bladder. Usually in persons with exstrophy of the bladder there are varying degrees of local inflammation, the result of mechanical and chemical irritation and infection. Associated ascending infection is common, and death usually is caused by toxemia of infection or of renal insufficiency. We have noted reports in the literature of nineteen cases of carcinoma complicating exstrophy of the bladder. Fourteen of these were of adenocarcinomas and two were of squamous-cell carcinomas; a histologic report was not included in three cases.

Although adenocarcinoma is of comparatively rare occurrence in the normal bladder, it is the type which most commonly occurs in exstrophy of the bladder. According to Young, adenocarcinoma comprises not more than 1 or 2 per cent of all the tumors of the bladder. In 369 tumors analyzed by Gardner,<sup>24</sup> four were diagnosed adenocar-

22. Von Geldern, C. E.: The Etiology of Exstrophy of the Bladder, *Arch. Surg.* 8:61 (part 1) (Jan.) 1924.

23. Johnston, T. B., quoted by von Geldern.

24. Gardner, J. A.: Clinical Results in Operations on Tumors of the Bladder by Various Operators for the Last Fifteen Years (A Review of 1,702 Cases). *Tr. Am. Urol. A.*, 1915, vol. 9, p. 165.

ing at certain points toward the vesical type and at others toward the intestinal type. Remedi<sup>17</sup> declared that certain glands derived from substrata completely foreign to either bladder or rectum become abnormal in early periods of life for unknown reasons and persist throughout life. Fornigginini concluded that while these theories are seductive, there is as yet no proof for the correctness of any of them, and that Enderlen's theory might be acceptable if it were based on observations in more than two cases.

#### ETIOLOGY

The ultimate cause of exstrophy of the bladder is not known. According to Young,<sup>18</sup> the existing theories collectively propose that this anomaly results from: (1) mechanical rupture; (2) pathologic lesions, or (3) defective embryonic development. The basis of the first conception is the assumption that the bladder ruptures from occlusion of the urethra. Hutchins and Hutchins<sup>19</sup> credited the origin of this conception to Bon and Duncan.<sup>20</sup> The adherents include Mueller, Rokitsky, Winckel, Brandl and Tiersch. Young pointed out that it fails to explain the associated epispadias and ununited pubes, and for these reasons the theory no longer has any proponents of note. Velpeau is said to have expounded the second hypothesis in which exstrophy of the bladder is interpreted as resulting from ulceration of the lower anterior abdominal wall, including the dorsal surface of the penis in the male, followed by the formation of adhesions. This theory does not explain the constant anatomic relations observed in this condition, and for this reason it likewise has been discarded. The adherents of the third hypothesis, that exstrophy is the final result of defective embryonic development of the bladder, include St. Hilaire, Meckel, Jaimain, Vialleton, Keibel, Gilis and others.

There are several modifications of the third hypothesis. Jaimain proposed that exstrophy of the bladder results from malunion in the median plane of the abdominal wall similar to that of the face in hare-lip. Kelly and Burnam<sup>21</sup> supported this view. Young expressed the belief, however, that this cannot be the cause, as the entodermal cavity from which the bladder is derived is closed from its beginning. Vialleton assumed that the cloacal membrane extends forward to an abnormal degree as a result of a primary defect in the abdominal wall, and that exstrophy results from the natural perforation of this mem-

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18. Young, H. H.: *Practice of Urology*, Philadelphia, W. B. Saunders Company, 1926, vol. 1, p. 538; vol. 2, p. 63.

19. Hutchins, E. H., and Hutchins, A. F.: *Exstrophy of Bladder with Successful Transplantation of Ureters into Rectum*, *Surg. Gynec. Obst.* 36:731, 1923.

20. Bon and Duncan, A., quoted by Hutchins and Hutchins.

21. Kelly, H. A., and Burnam, C. F.: *Diseases of the Kidney, Ureter and Bladder*, New York, D. Appleton & Company, 1914, vol. 2, p. 385.

attended dances and other social functions. She had never been able to control the flow of urine and had always worn napkins to collect it. The urine contained slight amounts of blood. Menstruation began at 14; the periods always had been regular but were associated with considerable pain. Two years before admission, local burning and aching appeared; this was increased on walking. The amount of

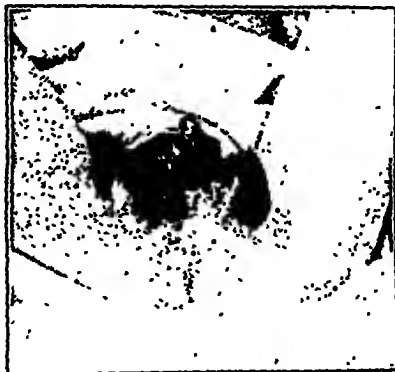


Fig. 8 (case 1).—Exstrophy of the bladder complicated by carcinoma.



Fig. 9 (case 1).—Excised bladder.

blood in the urine had increased. The bladder gradually had enlarged and usually was covered with slimy material with a foul odor. The patient had lost 20 pounds (9 Kg.) during the last two years.

The general examination gave negative results, except that the umbilicus was absent and a mass about 8 cm. in diameter on a broad pedicle projected from between the widely separated labia minora (fig. 8). The mass was covered with the tenacious mucoid discharge. It was extremely tender and bled on slight manipulation. Urine was seen to trickle from two points and menstrual blood

cinoma. There were nineteen (2.19 per cent) adenocarcinomas in 867 tumors of the normally developed bladder at the Mayo Clinic.

The mode of origin of adenocarcinoma in the normally developed bladder is not known. Young observed that the glands which are present in the mucosa of the normal bladder resemble the prostate and the glands of the prostatic urethra, and also that adenocarcinoma of the bladder commonly resembles carcinoma of the prostate. Verhoogan<sup>25</sup> added that adenocarcinoma of the bladder is encountered almost exclusively in the male. In contrast, the adenocarcinoma in exstrophy of the bladder usually resemble adenocarcinoma of the bowel; a considerable proportion occurs in females. Enderlen suggested that adenocarcinoma in exstrophy of the bladder results from metaplasia. This hypothesis is based on his conclusion that transitional epithelium is "normal" in exstrophy of the bladder since he found it in those of two new-born infants. Scholl expressed the belief that adenocarcinoma in exstrophy of the bladder results from a combination of metaplasia and hyperplasia. As we have pointed out, the presence of glandular tissue in most persons with exstrophy of the bladder in whom histologic studies have been made indicates that it is present normally.

From the embryologic considerations outlined, however, it seems logical to assume that the presence of glandular tissue in the bladder is a result of cell inclusion. The fact that both the bladder and the rectum are derived from the embryonic cloaca and the fact that exstrophy of the bladder is a congenital defect make this at least a reasonable assumption. Ehrich expressed this opinion in the statement that the bladder and intestines come from the same source, and that in their abnormal situation the tissues in exstrophy of the bladder have not the stimulus to assume normal transitional epithelium but retain that of the intestine. The occurrence of intestinal fistula complicating exstrophy of the bladder as in Keith's,<sup>26</sup> Hache's<sup>27</sup> and von Geldern's cases further demonstrates the close relation of the intestine to the bladder developmentally. Any attempt to explain the occurrence of adenocarcinoma in exstrophy of the bladder at least must consider these factors.

#### REPORT OF TWO CASES

CASE 1.—A woman, aged 38, came to the Mayo Clinic, Feb. 3, 1925, because of congenital deformity of the bladder. The deformity had caused little inconvenience until two years previously. As a child she had taken an active part in all games with other children; she had ridden a bicycle, and up to the last two years she had

25. Verhoogan, J.: *Neoplasmes de la vessie*, *Encycl. franç. d'urol.* 4:425, 1921.

26. Keith, A.: *Malformations of the Hind End of the Body*, *Brit. M. J.* 2: 1857, 1908.

27. Hache, Maurice: *Pathogénie et variétés de l'exstrophie de la vessie*, *Rev. de chir.* 8:218, 1888.



issued from a point posterior to the mass. The inguinal lymph nodes were enlarged. The urine contained albumin, blood and pus. Roentgenograms revealed congenital absence of the pubic bones. On the basis of these observations, a diagnosis of carcinoma complicating exstrophy of the bladder was made and was confirmed by biopsy.

The entire bladder was excised with the actual cautery (fig. 9). The right ureter appeared normal; fluid under pressure spurted from the left ureter, suggesting hydronephrosis. The ureters were drawn outside the wound and small retention catheters inserted. The pathologic diagnosis was adenocarcinoma of the bladder (figs. 10 and 11).

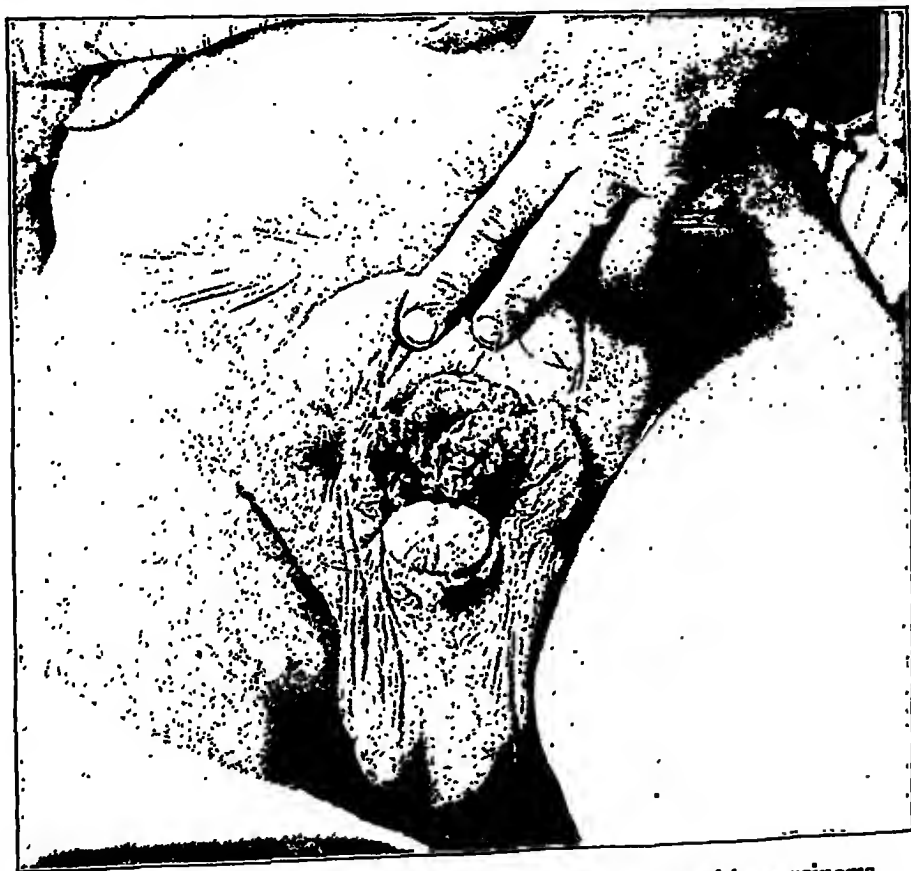


Fig. 12 (case 2).—Exstrophy of the bladder complicated by carcinoma.

The patient was advised to return for observation but did not do so until Feb. 1, 1928. At that time, her general condition was greatly improved. She had gained 40 pounds (18.1 Kg.). Examination revealed prolapse of the uterus; urine was not coming from the left ureter. There was no evidence of metastasis.

CASE 2.—A man, aged 48, came to the Mayo Clinic, Oct. 20, 1921, complaining of hemorrhages from the bladder. Exstrophy of the bladder had been present at birth. When he was 19, two plastic operations had been performed which were partially successful in enclosing the bladder. In 1920, he had had a mild stroke which temporarily affected the right side of the face and the right leg. In April, June and October of 1921 he had had hemorrhages from the bladder, on each occasion losing about a half pint of blood. He had lost 8 pounds (3.6 Kg.) since the first hemorrhage.



Fig. 10 (case 1).—Adenocarcinoma of the bladder;  $\times 150$ .



Fig. 11 (case 1).—Adenocarcinoma of the bladder;  $\times 350$ .

## ABSTRACT OF CASES

Case	Year	Author	Sex	Age	Lesion	Treatment	Comment
1	1895	Bergenhorn (quoted by Lecene and Hovelacque)	M	35	Adenocarcinoma	Transplantation of ureters; extirpation	Working 6 mos. after operation
2	1901	Ehrlich (Beitr. z. klin. chir. 30: 581, 1901)	F	44	Adenocarcinoma	Resection and transplantation of ureters and bladder mucosa	Died eighth day from ascending infection and uremia
3	1904	Enderlien (Verhandl. d. deutsch. path. Gesellsch. 7: 167, 1904)	F	38	Adenocarcinoma	Radiotherapy	Not benefited
4	1905	Lampe (Verhandl. d. deutsch. Gesellsch. f. Chir. 34: 226, 1905)	M	48	Squamous-cell carcinoma	Sonnenberg operation	Recovered; not traced
5	1906	Von Eiselsberg (Wien. klin. Wchnschr. 19: 548, 1906)	F	51	Adenocarcinoma	Extirpation	Living 15 mos. after operation
6	1909	Sargent (Brit. J. Chllo. Dis. 6: 115, 1909)	M	39	Clinically carcinoma	None	Not traced
7	1910	Wagner (Deutsche Ztschr. f. Chir. 104: 330, 1910)	M	49	Adenocarcinoma	Biopsy only	Not traced
8	1910	Hager (München. med. Wchnschr. 57: 2300, 1910)	M	60	Adenocarcinoma	Symptomatic	Died from cachexia
9	1910	Schloffer (Wien. klin. Wchnschr. 23: 1158, 1910)	M	46	Carcinoma	Curettage	Result not mentioned
10	1912	Lecene and Hovelacque (J. d'urol. méd. et chir. 1: 493, 1912)	M	48	Adenocarcinoma	Symptomatic	Died from cachexia
11	1912	Lecene and Hovelacque	F	57	Squamous-cell carcinoma	Previous nephrectomy	Died from cachexia
12	1914	Hunner (In Kelly and Burnam: Diseases of the Kidney, Ureter and Bladder, New York, D. Appleton & Co., 1914, vol. 2, p. 389)	F	26	Adenocarcinoma	Not mentioned	Result not mentioned
13	1918	Geraghty (In Cabot: Modern Urology, Philadelphia, Lea & Febiger, 1918, vol. 2, p. 208)	?	48	Adenocarcinoma	Not mentioned	Result not mentioned
14	1921	Lower (Ann. Surg. 73: 364, 1921)	M	50	Clinically carcinoma	Transplantation of ureters; excision	Result not mentioned
15	1922	Scholl (Ann. Surg. 75: 365, 1922)	F	23	Adenocarcinoma	Transplantation of ureters; excision	Died 2 years after operation from metastasis
16	1922	Scholl .....	M	48	Adenocarcinoma	Excision; radium	Reported well 6 years and 6 mos. later
17	1922	Dupont (J. d'urol. méd. et chir. 13: 433, 1922)	M	38	Adenocarcinoma	Exclusion of rectum	Died 2 days after operation
18	1924	Murphy (J. A. M. A. 82: 784 [March. 8] 1924)	M	49	Adenocarcinoma	Radium emanation	Examined after 14 mos.
19	1925	McCarthy and Klempner (J. Urol. 14: 419, 1925)	M	47	Adenocarcinoma	Dialthermy; ureterostomy; nephrectomy and cystectomy	Convalescent at time of report
20	1928	Judd and Thompson	F	38	Adenocarcinoma	Cautery excision of bladder	Well 3 years after operation

Examination revealed the exstrophy of the bladder to be partially covered by transplanted tissue (fig. 12). The mucosa of the bladder was hypertrophied, and it bled on slight handling. Bilateral inguinal hernia was present. The systolic blood pressure was 180 and the diastolic, 95.

The urine contained blood and albumin. The hemoglobin was 48 per cent, and the blood urea was 32 mg. for each hundred cubic centimeters. Roentgenograms revealed absence of the pubic bones. Dye was excreted normally from both ureters. The condition was diagnosed as carcinoma complicating exstrophy of the bladder and was confirmed by biopsy (fig. 13).

The mucosa of the bladder was completely excised. The thickened and dilated ureters were not disturbed. Radium was applied. The pathologist reported



Fig. 13 (case 2).—Adenocarcinoma of the bladder.

adenocarcinoma. On April 18, 1928, the patient reported that his general health was good.

(This case was reported previously by Scholl.)

#### COMMENT

Of the twenty cases reported, including the ones in the table, twelve occurred in men, seven in women, and in one case the sex was not mentioned. Two occurred in the third decade, five in the fourth, nine in the fifth, three in the sixth and one in the seventh. As stated, adenocarcinoma was reported in fifteen cases, squamous-cell carcinoma in two, and in three cases a histologic report was not made.

Surgical treatment was employed in ten of the twenty cases. In three, simple extirpation of the bladder was performed. In one case

# THE RELATIVE MECHANICAL STRENGTH OF ENTEROSTOMIES PERFORMED WITH AND WITHOUT CLAMPS

AN EXPERIMENTAL STUDY \*

R. A. CUTTING, M.D., PH.D.

NEW ORLEANS

Certainly many, perhaps most, of those members of the medical profession whose interest leans toward surgery, especially abdominal surgery, have a fairly well defined mental reaction either in favor of or opposed to the use of clamps in intestinal work. On the one hand, there are those who believe that the use of clamps is a pernicious practice and one which should be generally abandoned, while, on the other hand, there are those who feel that for one reason or another the technic in which clamps are used is preferable to a clampless method; still others believe that the use of clamps should perhaps be confined to the occasional or relatively unskilful operator; while a clampless technic should be the goal of the finished surgeon.

Though there have appeared in the literature over a number of years various studies which have pointed out some of the possible unfavorable sequelae of the use of clamps in intestinal operations, especially the occurrence of hematomas and postoperative ulceration, direct experimental attacks on some of the other aspects of the problem, especially the relative mechanical strength of enterostomy wounds made with and without clamps, have not, to my knowledge, been subjected to systematic investigation.

The experiments to be reported in this paper were undertaken primarily to elucidate the question of mechanical strength, but an attempt was made at the same time to observe and record a few other phenomena which might present some bearing on the general question of the advisability or inadvisability of the use of clamps in intestinal operations.

## TECHNIC EMPLOYED

*Recording Pressure.*—It has been assumed, for purposes of the present investigation, that the pressure required to burst the intestinal wall is an accurate measure of the mechanical strength of the latter, and for recording bursting pressures the mercury manometer has been accepted as the standard of measurement.

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\* From the Department of Surgery, Tulane University of Louisiana School of Medicine.

(reported by Scholl), transplantation of the ureters by the Mayo<sup>28</sup> method preceded removal of the bladder. The patient died two years after the operation from metastasis. In the two cases reported here, the patients are alive and well three and six and a half years, respectively, after operation. Von Eiselsberg's patient was living and well fifteen months after extirpation of the bladder. In three other cases transplantation of the ureters into the colon was performed. One of these patients died eight days later from uremia following ascending renal infection. In the other two cases, resection of the bladder was performed secondarily. In one case, the patient was well and working six months after operation; in the other case, the result was not stated. In one case nephrectomy, abdominal ureterectomy and cystectomy were performed; the patients were recovering from these operations at the time the report was made. In one case the Sonnenberg operation was performed; the patient recovered but was not traced afterward. In one case exclusion of the rectum was attempted, from which the patient died. Radium was applied in two cases as the only treatment; one of the patients was well after fourteen months, but the other was not improved. Six patients either did not receive treatment or were given symptomatic treatment only, and in two cases the treatment was not mentioned. Three of the six patients died from cachexia; two were not treated because of bad prognosis, and the result was not stated with regard to the other.

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28. Mayo, C. H.: *Exstrophy of the Bladder and its Treatment*, J. A. M. A. 69:2079 (Dec. 22) 1917; *Exstrophy of the Bladder, Contribution to Medical and Biologic Research*, New York, Paul B. Hoeber, 1920, p. 1095; *The Formation of a Cloaca in the Treatment of Exstrophy of the Bladder*, Surg. Clin. N. Amer. 1:1257, 1921. Mayo, C. H., and Hendricks, W. A.: *Exstrophy of the Bladder*, Surg. Gynec. Obst. 43:129, 1926. Mayo, C. H., and Walters, Waltman: *Transplantation of Ureters into Rectum: End-Results in Thirty-Five Cases of Exstrophy of Bladder*, J. A. M. A. 82:624 (Feb. 3) 1924.

the rubber tubing in the latter part of the apparatus, the stem of the inner tube of an automobile with its contained air valve was introduced, so as to prevent reflux of air from the system to the pump, once the plunger of the latter had initiated its action. Such an apparatus, though somewhat ungainly in size, was found not to have an undue reserve capacity in cases in which the bursting pressure required was near normal, and by the exercise of a little care it was found feasible to increase the pressure in the system up to the point of rupture of segments of intestine with a fair degree of rapidity and without causing much oscillation in the columns of mercury. It was considered that the bursting pressure of a segment of intestine might vary with the interval of time during which it was required to withstand the development of the pressure; accordingly, when the ruptures were performed, air was forced into the system as rapidly as could be done without inducing oscillation of the mercury columns and as steadily as possible. The intestinal wall was required to withstand pressure for about ten seconds under these circumstances, and the pressure at which the rupture occurred could be determined with an accuracy well within 5 mm.; an attempt was not made, however, to estimate more accurately than 5 mm., since the pressure magnitudes in every case brought the margin of error under these conditions well within an experimental error of 5 per cent, which could hardly be considered of serious moment in a consideration of end-results under the contemplated experimental conditions. An error of 5 per cent, however, as here mentioned, must be regarded as the maximum, since in most cases a difference of 5 mm. in recording a given pressure represents a far smaller variation in percentage than even a half of this, i.e., 2.5 per cent, since the magnitudes recorded are in nearly all cases more than 200 mm. In some cases, an error of 5 mm. in reading would represent less than one-half of 1 per cent.

Sections of intestine to be tested for bursting were cut so as to measure approximately 5 inches (12.7 cm.) in length in all cases, including those which were made to include an operative enterostomy opening.

*Operative Procedure.*—The operative procedures were performed under strictly aseptic conditions, under general ether anesthesia by the open drop method and without preliminary narcosis. A high right rectus incision, about 6 cm. long, was employed; after the skin, subcutaneous tissues and rectus sheath had been incised, the belly of the rectus muscle was retracted laterally and the incision completed through the posterior sheath and peritoneum in the line of the incision in the skin; the omentum was pulled upward and displaced to the left, and a loop of jejunum, as near the duodenum as convenient, was delivered through the abdominal wound. Two lateral anastomoses were made in each animal between the limbs of such loops without interrupting the continuity of the lumen around the communicating bend, dependence being placed on the kinking of this area to produce sufficient obstruction to insure the patency of the enterostomy opening (fig. 2), a form of obstruction which proved to be adequate in all cases. Both anastomoses were performed according to exactly the same technic as far as was humanly possible, with the single exception that one was performed with the aid of light intestinal clamps, while the other was performed with the aid of "guy sutures." The clamps used were of the double bladed "Doyen" pattern and were covered with rubber tubing; they were applied solely for purposes of approximation of loops and control of intestinal leakage. The pressure exerted by them was never made so great as to produce any considerable degree of hemostasis or local anemia.

Preliminary tests with sections of intestine removed from dogs recently killed in the course of other experiments showed that it might be necessary in the course of these experiments to record pressures well over 1,000 mm. of mercury; accordingly, a 4 foot manometer was constructed by bending glass tubing in the shape of a U, mounting it on a wooden support, as illustrated in figure 1, and filling it to a depth of 2 feet (61 cm.) with metallic mercury. To one arm of the manometer was attached a piece of fairly stiff-walled rubber tubing, about 3 feet (91 cm.) long, and to the other end of the tubing

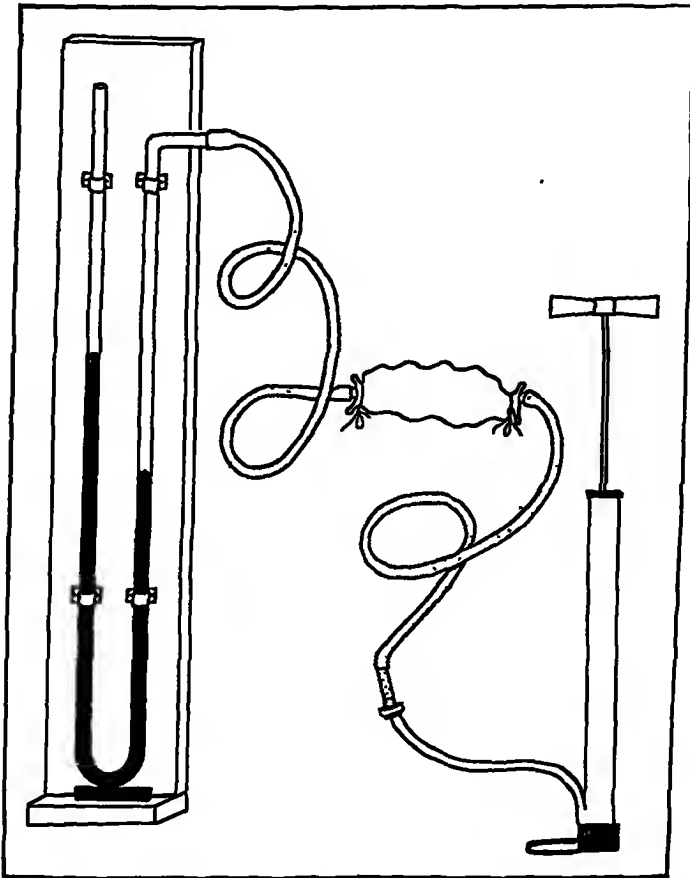


Fig. 1.—Apparatus used for introducing air pressure into segments of intestine and for measuring the pressure required to burst these segments. An automobile tire pump forces air through the valve stem of an inner tube with its contained air valve and thence through rubber tubing to the segment of intestine; the other end of the intestinal lumen connects by rubber tubing with one arm of a large mercury manometer.

was fitted a short piece of glass tubing over which a segment of intestine might be slipped and subsequently tied. Air pressure was introduced into the other end of the segment of intestine by means of an automobile tire pump connected by means of another length of rubber tubing and a glass end piece over which the free end of the intestinal segment might be fitted and tied as before. As a connection between the regular screw cap of the tire pump and



"loop on the mucosa" or "Connell" stitch; the third line of sutures was completed with the "right-angled stitch of Cushing," and the fourth line, the continuation of the first line, was also an "anti-leak" right-angled stitch. Needles swedged onto chromicized catgut were used in suturing the second and third suture lines to minimize trauma, but an ordinary intestinal needle was used to carry the silk.

White silk was used to distinguish those entero-enterostomies which were made with "guy sutures," while black silk was used to distinguish those made with clamps. Variations in technic, such as extra sutures at possible weak points, were never permitted, nor was unusual technical care allowed in the case of any animal. The aim throughout the experiments was to approximate the same degree of care taken under actual working conditions in hospital routine. I myself performed all of the procedures with the help of a laboratory technician, previously trained as a nurse, as assistant, and a laboratory diener as anesthetist. The time consumed in performing the operations varied from an hour to an hour and a half or was occasionally longer in cases in which considerable troublesome hemorrhage was encountered.

An attempt was not made to keep a record of the exact operative time, since any attempt to do so might unconsciously have acted as an incentive to a betterment of previous records and so have predisposed to unwise haste. Postoperatively, the animals did not receive food for twenty-four hours, but were allowed all the water they wanted; feedings of milk were given on the second day, and bread and meat were added to the diet on the third and subsequent days.

*Number and Selection of Animals.*—In experimental work, one is always somewhat at a loss to know just how many animals should be used for any given experimental series, and the decision must ultimately depend on a number of factors. In this series twenty-nine animals were used, three of which were not included in the final series, for reasons which will be given presently; the plan followed was to operate and perform autopsy on two animals for each successive postoperative day for twelve days, making observations on two dogs directly after operation, and extending the series, by daily autopsies on two dogs, so as to include twelve postoperative days. It was considered that such a series would prove large enough to establish any facts of signal significance, on the one hand, and would, on the other, avoid taxing the experimenter too sorely from the operative point of view.

It was considered advisable in performing these operations to attempt to overcome the factor of possible increasing operative skill, as the series progressed, by the simple expedient of allowing the animals to fall into the series in a haphazard manner; in some of the animals which were operated on early in the series autopsies were performed relatively late, and vice versa; accordingly, the distribution as to operative date will be noted to be virtually a chance distribution.

The course of the investigation extended over a period from Nov. 9, 1927, to March 29, 1928, as shown in table 1.

Since the possible influence of the sex and size of the animals could not be predetermined, and the matter of age, etc., was practically uncontrollable in any case, animals of both sexes and of various sizes, breeds, ages and conditions were selected at random, one enterostomy with clamps and another without clamps being performed on the same animal at a single operation; the enterostomies were performed close together in the same part of the

it being assumed that macération, or even temporary strangulation of tissue, is never a desideratum in operations, but rather an occasionally necessary evil in those cases in which it is allowed to occur; further, such trauma should be of only accidental occurrence in intestinal operations.

In the operation in which clamps were used, the latter were applied to one loop of jejunum, after it was freed of intestinal contents by being milked gently between the gloved fingers, and then a similar clamp was applied to an adjoining loop in the same fashion; both clamps were subsequently brought into such position as to oppose antimesenteric borders for convenient suturing, the clamps then being held in position by two pieces of gauze introduced in



*Standards of Comparison.*—The enterostomies were made high in the jejunum in all cases; the exact distance from the pylorus could not be measured at operation, but the variation in the series was not great at autopsy, as shown in table 2.

TABLE 2.—Distance from Pylorus to First Entero-Enterostomy  
(Measured at Autopsy)

Dog	Inches	Dog	Inches	Dog	Inches
1.....	.18	13.....	.12	22.....	.14
2.....	.14	14.....	.14	23.....	.14
3.....	.10	15.....	.12	23.....	.15
6.....	.15	16.....	.13	24.....	.12
7.....	.16	17.....	.15	25.....	.11
8.....	.16	18.....	.18	26.....	.11
9.....	.9	19.....	.13	27.....	.12
10.....	.12	20.....	.15	28.....	.18
12.....	.12	21.....	.16	29.....	.12

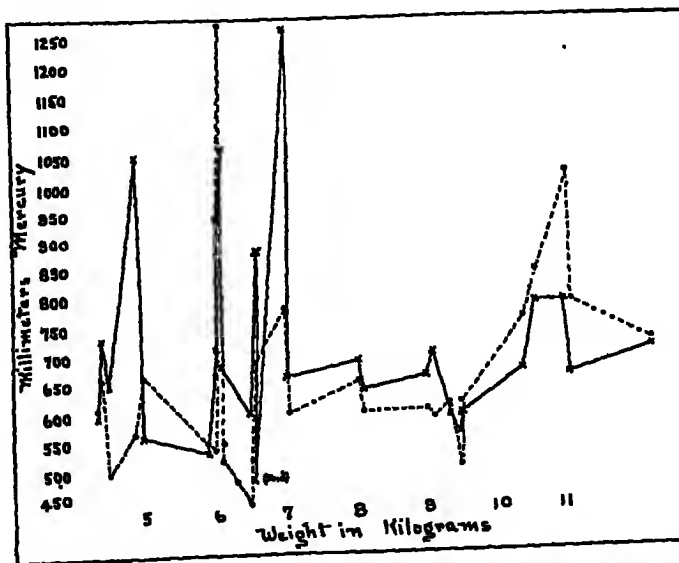


Fig. 3.—Graphic representation of the bursting pressure of segments of intestine removed just cephalad (broken line) and caudad (solid line) to the entero-enterostomies, in relation to the weights of the dogs used. The bursting pressures of the caudad segments average 7.4 per cent higher than those cephalad, but the bursting pressures do not bear any evident relation to the weights of the animals.

The pressure required to burst normal intestine in this region (i.e., the upper jejunum) was found by excising two segments of intestine, one just proximal to the two entero-enterostomies and the other just distal; these were burst and averages were made of the two bursting pressures. That this represents the true normal bursting pressure in animals not operated on is, of course, questionable, since the adjacent operative procedure may well have affected these segments also. To estimate the percentage of strength of the two intervening entero-enterostomies, the bursting pressure for each was measured and the percentage of strength computed as a decimal fraction by dividing this pressure by the average normal pressure previously determined.

intestine, in an attempt to make conditions as directly comparable as possible for a given animal. Under such conditions, the two minor variables—(1) the order in which the anastomoses were performed, i.e., whether the technic with clamps or that without clamps was used first, and (2) the order in which the operations occurred in the intestine, i.e., whether oralward or analward—in a given type were considered. It was decided that such variables could best be overcome (a) by performing the technic first with clamps in one half of the series and first without clamps in the other half, and (b) by allowing the order with respect to the direction of flow of intestinal contents to vary accord-

TABLE 1.—*Data of Investigations*

Dog	Sex	Weight, Kg.	Date of Operation	Date of Autopsy	Postoperative Days
1	F	6.3	11/ 0/27	11/19/27	10
2	F	8.1	11/ 9/27	11/18/27	9
3	F	11.0	11/18/27	11/25/27	7
4*	F	5.2	11/24/27	11/28/27	4
5*	M	12.5	11/24/27	11/28/27	4
6	M	6.2	12/ 0/27	12/12/27	0
7	M	9.5	12/ 0/27	12/13/27	7
8	F	0.0	12/ 9/27	12/15/27	6
9	M	7.1	12/ 9/27	12/17/27	8
10	F	7.0	12/21/27	12/23/27	2
11	M	0.2	12/23/27	12/25/27	Died
12	F	4.5	12/27/27	12/29/27	2
13	F	4.3	12/28/27	12/30/27	1
14	F	11.2	2/15/28	2/26/28	11
15	M	8.2	2/20/28	2/24/28	4
16	F	5.8	2/20/28	2/24/28	4
17	M	5.0	2/23/28	3/ 1/28	1
18	M	10.4	2/22/28	3/ 3/28	10
19	M	0.5	2/22/28	3/ 2/28	9
20	F	10.6	2/20/28	3/ 3/28	8
21	M	0.2	3/16/28	3/24/28	8
22	M	14.4	3/17/28	3/29/28	12
23	M	11.1	3/20/28	3/25/28	5
24	M	6.0	3/20/28	3/31/28	11
25	F	4.8	3/21/28	3/24/28	3
26	M	6.1	3/21/28	4/ 2/28	12
27	F	4.4	3/23/28	3/23/28	0
28	M	0.2	3/23/28	3/28/28	5
29	M	6.5	3/20/28	3/29/28	0

\* Dog 11 died on the second postoperative day of general peritonitis. Dogs 4 and 5 were both operated on the same afternoon, and four days later were living and apparently normal; at autopsy, however, they each showed a small area of suppuration at the suture line, which was apparently well walled off by adhesions, but which rendered the animals unfit for the purpose of these experiments. Apparently some unrecognized lapse in aseptic technic occurred on this particular afternoon.

ing to chance. The animals numbered from 1 to 13 are those in which the technic with clamps was performed before that in which "guy sutures" were used, and the animals from 14 to 29 represent the reverse. At operation, an attempt was not made to determine the direction of intestinal flow in a selected loop, and so a record was not made at the time of operation as to the space order (proximal or distal) in which the enterostomies were made; at autopsy it was also frequently impossible to determine what the space order was, until after the loops had been cut apart and burst so as to reveal the identifying silk sutures; by this time there was often a question as to just what the arrangement had been previously, so that attempts to make observations on this particular feature, even at autopsy, were abandoned early.

frequently show the reverse. The occasional considerable variation in bursting pressure between the proximal and distal segment is also interesting.

Figure 4 represents graphically the relation between the strength of the normal intestine and the sex of the animals. Thirteen males and thirteen females are represented, although this equal sex distribution occurred by chance. On the whole, the bursting pressure of the female intestine is greater than that of the male, weight for weight, though here again there are many exceptions.

*Position and Character of Rupture of Normal Intestinal Segments.*—Table 3 shows in detail the position and character of the ruptures which occurred in segments of normal intestine.

Three general varieties were noted: (1) the rupture at the antimesenteric border, by far the most common variety; (2) rupture at the mesenteric border, of much less frequent occurrence, and (3) intermediate rupture, a still less frequent variety, which occurred between the mesenteric and antimesenteric borders.

Bursting of the most common, or antimesenteric, type occurred in 74.1 per cent of the cases, of which a few presented a more or less slow leak (5 per cent), while by far the greatest number (69 per cent) presented diffuse bursting with explosive violence. In the latter the bursting usually involved a more extensive rupture of the submucosa and mucosa than of the peritoneal coat, so that the peritoneal coat characteristically extended, stretched but unbroken, over considerable areas of the underlying ruptured tunics; occasionally, however, the rupture of all tunics was coextensive. The length of rupture of all coats varied from half an inch to the entire length of the segment in some cases. The explosion usually rivaled the detonation of a giant firecracker.

Mesenteric rupture was noted in 17.2 per cent of the cases and presented the same two subtypes as noted previously, i. e., (a) slow leak (6.8 per cent) and (b) diffuse explosive rupture (10.3 per cent); the explosive force and extent of the mesenteric rupture was always, however, less than that of the antimesenteric variety. The type called "intermediate" occurred in 8.9 per cent of the cases, of which half (two cases) presented slow leaks, and the other half, diffuse rupture.

*Place of Rupture of the Entero-Enterostomy Opening.*—Table 4 shows the places at which rupture of the various entero-enterostomies occurred; since the table represents so many different postoperative time intervals, it is difficult to interpret and probably should not be interpreted closely.

The place of rupture in most cases is apparently the point of maximum mechanical strain. In only four cases in the series was rupture

## RESULTS

The results have been tabulated and reproduced. Figure 3 represents the various bursting pressures of the caudal and cephalad segments of the normal jejunum removed, as previously described, from just above and just below the entero-enterostomies. It is interesting to note that the bursting pressure of the distal or caudal segment averages nearly 7.5 per cent stronger than that of the proximal segment, the distance of intestine intervening between the two being approximately 10 inches (25.4 cm.). Expressed in millimeters of mercury, the average difference is 39.2 mm., which is certainly a significant difference. Whether the presence of the intervening entero-enterostomies is to be considered as the cause of this difference in bursting pressure or whether the difference is inherent in the intestine of the normal animal cannot, as previously suggested, be determined from these experiments.

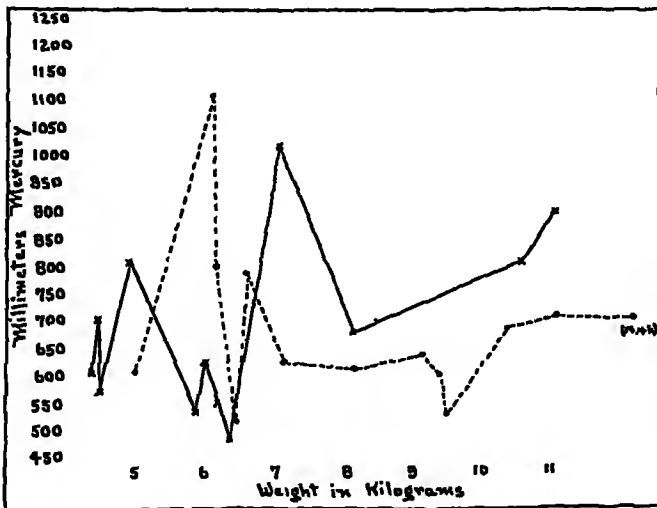


Fig. 4.—Graphic representation in which the bursting pressures of both cephalad and caudad segments are averaged and plotted with respect to the sex of the animals used. There is a slight but distinct trend toward greater strength in the female intestine. The solid line indicates females and the broken line, males.

It is also interesting to note in connection with this graph that the strength of the segments of normal intestine does not bear a simple relation to the weight of the animal. Possibly, on the whole, there is a slight tendency for the bursting pressure of the intestine of larger dogs to be greater, and that of smaller dogs to be less, but the exceptions are so numerous and of such magnitude that one is hardly justified in drawing such a conclusion from this series of animals. On the contrary, it is probably not without significance that occasionally, at least, small dogs have high intestinal bursting pressures, while larger dogs

through the normal intestinal wall noted, and these cases all fell within the postoperative interval of eight to ten days. That rupture at the angle of the suture line did not occur more frequently probably cannot be interpreted as meaning that this point was unusually strong, but rather that the particular way in which the enterostomies were made tended to throw stress along the side of the entero-enterostomy rather than at the angle.

The crux of the investigation is represented in figures 5 and 6 and concerns the relative strength of the enterostomies themselves as con-

TABLE 4.—*Position of Rupture of Entero-Enterostomies*

Dog	With Clamps			Without Clamps		
	Near Angle of Suture Line	Along Side of Suture Line	Outside Suture Line	Near Angle of Suture Line	Along Side of Suture Line	Outside Suture Line
1	..	..	+	+	..	..
2	..	..	+	+	..	..
3	..	+	..	..	+	..
6	+	..	..	..	+	..
7	..	+	..	+	..	..
8	+	..	..	+	..	..
9	..	+	..	..	..	+
						(8 days)
10	+	..	..	..	+	..
12	+	..	..	..	+	..
13	..	+	..	+	..	..
14	+	..	..	+	..	..
15	..	+	..	..	+	..
16	..	+	..	..	+	..
17	..	+	..	..	+	..
						(10 days)
18	..	..	+	+	..	..
19	..	+	..	..	+	..
20	+	..	..	..	+	..
21	..	+	..	..	+	..
22	+	..	..	..	+	..
23	..	+	..	+	..	..
24	..	+	..	..	+	..
25	+	..	..	+	..	..
26	..	+	..	..	+	..
27	+	..	..	+	..	..
28	+	..	..	..	+	..
29	..	+	..	..	+	..

lence of the animals proceeded. Two bursting pressures are plotted for each postoperative day; the solid black blocking at the bottom of the graphs represents the lesser bursting pressure and the lighter blocking above, the greater bursting pressure of each of two animals. Immediately following the operation, performed by either method, the enterostomies show a strength roughly between 20 and 40 per cent of that of the normal intestine; with both methods, for the first three days, the strength progressively decreases to a minimum on the third day of roughly between 15 and 25 per cent, and on subsequent days the strength progressively rises to a maximum, about the tenth day, of between 90 and 110 per cent of normal, the normal intestine rather than the enterostomy occasionally rupturing toward the end of this period. On

TABLE 3.—*Position and Character of Rupture of Segments of Normal Jejunum Oral Segment*

Dog	Diffuse Antimesenteric (Explosive)	Antimesenteric (Slow Leak)	Diffuse Mesenteric (Explosive)	Mesenteric (Slow Leak)	Intermediate (between Antimesenteric and Mesenteric Borders)
1	..	..	..	..	+ (slow leak)
2	+	..	..	..	..
3	+	..	..	..	..
6	..	..	+	..	..
7	+	..	..	..	..
8	..	..	..	+	..
9	..	..	..	..	+ (diffuse explosive)
10	+	..	..	..	..
12	+	..	..	..	..
13	+	..	..	..	..
14	+	..	..	..	..
15	+	..	..	..	..
16	..	..	+	..	..
17	+	..	..	..	..
18	+	..	..	..	..
19	+	..	..	..	..
20	..	..	+	..	..
21	..	+	..	..	..
22	+	..	..	..	..
23	..	..	+	..	..
24	..	..	..	+	..
25	+	..	..	..	..
26	+	..	..	..	..
27	..	..	..	..	+ (slow leak)
28	+	..	..	..	..
29	+	..	..	..	..
Total	18	1	4	2	8

<i>Aboral Segment</i>					
1	+	..	..	..	..
2	..	..	..	+	..
3	+	..	..	..	..
6	..	..	+	..	..
7	+	..	..	..	..
8	+	..	..	..	..
9	+	..	..	..	..
10	..	+	..	..	..
12	+	..	..	..	..
13	..	..	..	..	+ (explosive)
14	+	..	..	..	..
15	+	..	..	..	..
16	+	..	..	..	..
17	+	..	..	..	..
18	+	..	..	..	..
19	+	..	..	..	..
20	+	..	..	..	..
21	+	..	..	..	..
22	..	+	..	..	..
23	+	..	..	..	..
24	+	..	..	..	..
25	+	..	..	..	..
26	+	..	..	..	..
27	+	..	..	..	..
28	..	..	+	..	..
29	+	..	..	..	..
Total	22	2	2	1	1



the eleventh day, however, the strength of the enterostomies has again decreased to approximately half of normal, but on the following, or twelfth day, seems again to be on the increase. When one compares the strength of those enterostomies performed with clamps with the strength of those performed with "guy sutures," as shown in figure 7, it is seen that not much difference is to be found, though if anything, the technic employing clamps seems to yield a stronger entero-enterostomy, especially at the critical period, i. e., when the operative anastomosis is weakest, between the second and fourth days. In this connection, it should be noted that the graphs are made on the basis of percentage strength, rather than on that of millimeters of mercury; 1 per cent on the graph represents, on the average, 5.85 mm. of mercury.

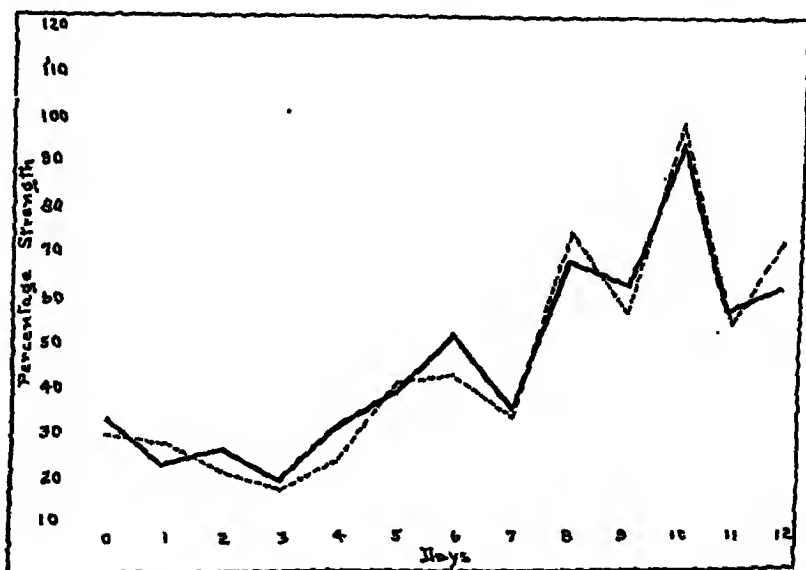


Fig. 7.—Graphic representation in which the bursting pressure of gastro-enterostomies performed with clamps is plotted against the bursting pressure of those performed without clamps (i.e., with "guy sutures") over a period of twelve postoperative days. Each day is represented by averaging the results from two dogs, four enterostomies being plotted for each day—two with clamps and two without. The entero-enterostomies performed with clamps are slightly stronger than those performed without clamps, the greater strength being apparent on the second, third and fourth days during which the entero-enterostomies performed by both methods are weakest.

These results check fairly well with the experiments of Chlumsky,<sup>1</sup> who found the bursting pressure of entero-enterostomies in dogs to be (1) one third of that of the normal intestine immediately after operation; (2) to decrease progressively for four days to one third of the latter pressure; (3) to rise progressively to their original strength

1. Chlumsky, quoted by Bartlett: *After Treatment of Surgical Patients*, St. Louis, C. V. Mosby Company, 1920, vol. 2, p. 810.

# CUTTING—ENTEROSTOMIES

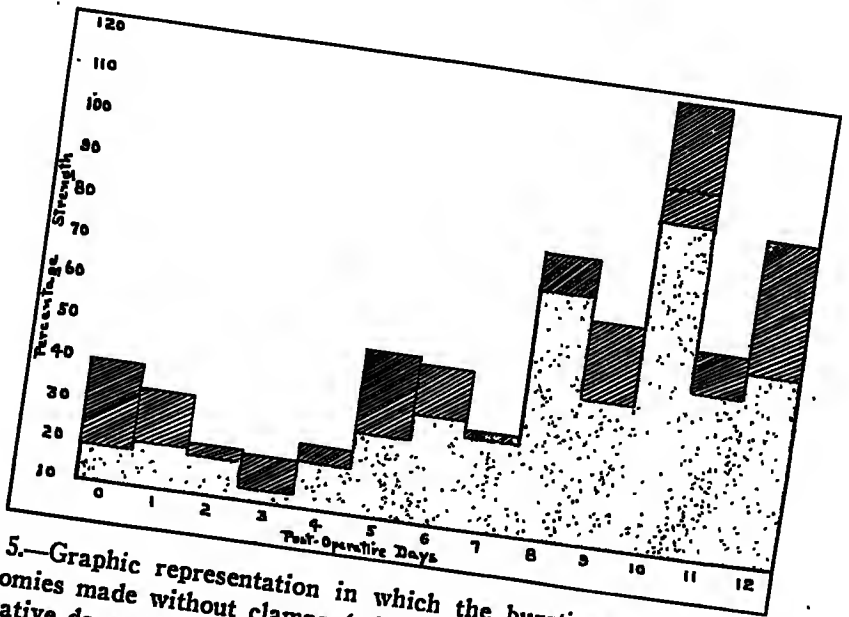


Fig. 5.—Graphic representation in which the bursting pressure of enterostomies made without clamps (with "guy sutures") is plotted for twelve postoperative days, two observations being plotted for each day. The bursting pressure declines for the first three days, rises for the next seven days and declines again during the last two days.

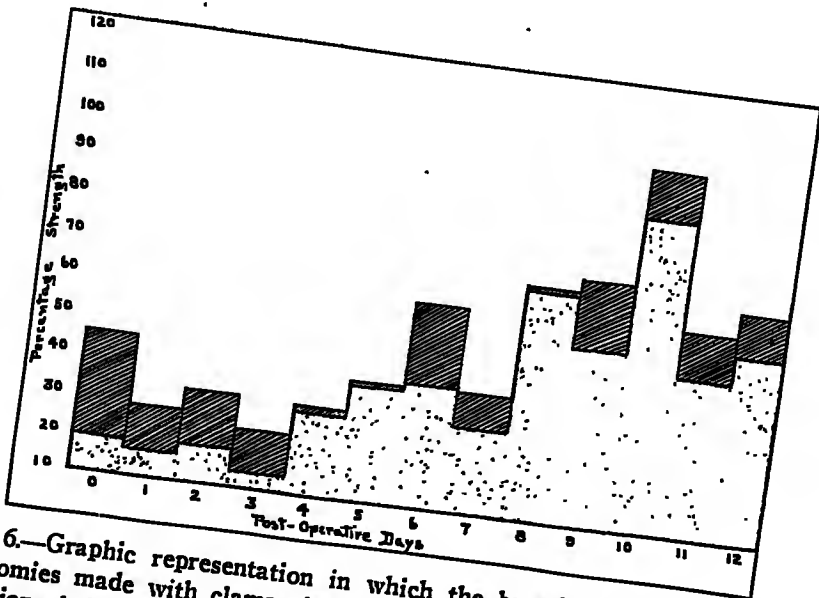


Fig. 6.—Graphic representation in which the bursting pressure of enterostomies made with clamps is plotted for twelve postoperative days, two observations being plotted for each day. The bursting pressure declines for the first three days, rises for the next seven days and declines again during the last two days.

# TRAUMA AS A FACTOR IN ACUTE APPENDICITIS

ADDISON H. BISSELL, M.D.

STAMFORD, CONN.

Because of the many instances in which compensation has been denied, trauma as a factor in producing appendicitis deserves attention. The pathologic evidence agrees with well known experimental observations. When there is a history of trauma to the abdominal wall, followed by symptoms and signs of peritoneal irritation, the examiner should bear in mind the possibility of an inflammation of the appendix. Von Neumann<sup>1</sup> reported that trauma plays a part in the cause of acute appendicitis in 6.6 per cent of the cases. The four cases reported here occurred in 101 appendectomies, making trauma an etiologic factor in 4 per cent.

The Idaho Commission<sup>2</sup> said that appendicitis from strain is not a probability, and rarely, if ever, occurs.

In a case<sup>3</sup> which occurred in California, the employee suffered a strain while lifting heavy objects, and felt a severe abdominal pain. Autopsy six days later revealed a ruptured gangrenous appendix. Expert testimony was to the effect that this was merely a coincidence. In numerous other incidences, employers have contended that appendicitis is not caused by trauma.

Many cases of traumatic appendicitis have been reported by Smith,<sup>4</sup> Soresi,<sup>5</sup> Sherrick<sup>6</sup> and others. Deaver<sup>7</sup> said he had "never seen a case of acute appendicitis in which injury was alleged as the direct exciting cause in an appendix that did not show some evidence of previous disease. It is well known that foreign bodies, fecal concretions, strictures of the appendix, and adhesions, are frequently present without giving the patient any trouble or suggestion of a lesion in the right iliac fossa."

The experiments of Furbinger and von Hanseemann<sup>8</sup> showed that they were able to express the contents of a full cecum into the appendix by light manual pressure over the cecum and ascending colon, and by

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1. VonNeumann, quoted by Choyce: *System of Surgery*, New York, Funk & Wagnalls Company, 1912, p. 541.

2. Research Report no. 61 National Industrial Conference Board, August, 1923, p. 133.

3. *Murphy v. Southwest Shipbuilding Co. Cas. Industrial Com. Decisions*, vol. 7, p. 114.

4. Smith: *Brit. M. J.* 1:283, 1923.

5. Soresi: *M. Rec.* 99:718, 1923.

6. Sherrick: *Illinois M. J.* 2:153, 1915.

7. Deaver: *New York M. J.* 85:1105, 1907.

8. Furbinger and von Hanseemann, in Ludington, N. A.: *Etiology of Traumatic Appendicitis*, *J. A. M. A.* 80:1448 (May) 1923.

on the seventh day, and (4) to equal the intact intestinal wall on the tenth day. According to the present experiments, however, as already noted, the bursting pressure is lowest on the third and not the fourth day, it supersedes the original bursting pressure on the fifth and subsequent days, rather than merely reaching such pressure on the seventh day and shows a marked decrease on the eleventh day, which Chlumsky did not note.

#### CONCLUSIONS

1. A constant relationship does not exist between the weight of a dog and the bursting pressure of its upper jejunum, the intestine of larger dogs often showing relative weakness and that of smaller dogs relatively extreme strength.

2. Under the conditions of these experiments, segments of the upper jejunum 12 inches (30.4 cm.) or more cephalad to other segments show an average difference of bursting pressure of more than 7 per cent in favor of the distal segment.

3. The jejunum of female dogs is slightly stronger than that of males, weight for weight.

4. Entero-enterostomies performed by both "clamp" and "clampless" technics are about one-third as strong as normal intestine immediately after they are performed; they progressively decrease in strength for three days, then rapidly and progressively increase in strength up to, or exceeding, the strength of normal intestine by the tenth day, then suddenly fall again to about 50 per cent of the intact intestine on the eleventh day, and on the twelfth are again on the ascent.

5. Entero-enterostomies performed with clamps, when the latter are used merely for purposes of "approximation of the parts and for control of intestinal leakage" are, if anything, slightly stronger than ones performed with "guy sutures," especially on the second, third and fourth postoperative days, which constitute the critical period.

6. Entero-enterostomies performed by either method and on all postoperative days, up to and including the twelfth, showed marked variations in strength, even though operative technic was kept as constant as humanly possible and postoperative care was the same in all cases, variations exceeding 100 per cent being noted frequently in the early three or four days and variations of the order of magnitude of 50 and 75 per cent being common throughout the entire twelve days.

7. The normal upper jejunum ruptures most characteristically (i. e., in about three fourths of the cases) at its antimesenteric border, though less frequently it ruptures at its mesenteric border, and occasionally at a point intermediate between the two; the characteristic rupture is a diffuse one with explosive violence and involves the mucosa and submucosa more extensively than the serosa.

To argue as to whether the organ was normal or not is beside the point, for the abnormalities that make for easy invasion of the appendix by infection after injury are compatible with good health, and often impossible to diagnose. The question should be whether an abdominal injury, or unusual strain, can precipitate the clinical picture of acute appendicitis? There does not seem to be any doubt that this can take place. The trauma is the deciding factor.

#### REPORT OF CASES

CASE 1.—O. G., aged 14, who had not had any previous attacks of appendicitis, while playing football two days before admission fell forward striking his abdomen on a rock. He felt severe abdominal pain immediately and vomited. The abdominal pain was severe at first, was somewhat lessened after an hour, but was constantly present to the time of operation. On the second day, his physician brought him to the hospital, where I performed an emergency operation on May 21, 1924. The wall of the cecum was injected and thickened. The right iliac fossa was the site of a large abscess, and free in this abscess was a concretion. The appendix was long, coursing down and in over the pelvic brim, and its distal half was necrotic. The whole appendix was acutely inflamed. Near the tip there was a perforation 1 inch (2.5 cm.) long opposite the attachment of the mesentery. Appendectomy with drainage was performed. The patient recovered.

CASE 2.—R. S., aged 10, without any previous history of appendicitis, received a severe kick in the abdomen while playing football. He felt immediate abdominal pain, was nauseated and vomited. He "felt faint" in the upright position, and was chilly. He was kept in bed at home for six days without being seen by a physician and suffered constantly from severe abdominal pain, nausea, vomiting, chills, distention and constipation. On the sixth day, he was sent by a physician to the hospital, where I performed an operation immediately on Sept. 24, 1925. A marked generalized fibrinopurulent peritonitis was present. The appendix was 3 inches (7.6 cm.) long and necrotic throughout. Near the tip there was a perforation 1 inch (2.5 cm.) long, with markedly thickened, everted edges. A large concretion was found in the pus near the perforation, which was on the external lateral aspect of the appendix. Appendectomy with drainage was performed, and the patient recovered. There was fecal drainage in decreasing amounts for five days.

CASE 3.—T. F., aged 19, who had not had any previous attacks of appendicitis, forty hours before operation was performed, had been thrown on his back while wrestling, and his opponent had jumped on his abdomen. The patient said that he "felt something crack" in his abdomen, and felt immediate colicky abdominal pain. For an hour or so, he was nauseated. The colicky pain, which was not severe, kept up constantly until twelve hours after injury when all his symptoms became much worse, and were localized in the right lower quadrant. He vomited frequently, complained of being chilly and, after twenty-four hours, became delirious at times. Forty hours after the injury occurred, he was brought to the hospital, where I performed an emergency appendectomy on April 27, 1926. The appendix was 4 inches (10.16 cm.) long, in normal position, and was not adherent. The entire appendix was markedly inflamed, and the distal half was necrotic. There was a perforation 1 inch (2.5 cm.) long near the tip on the antimesentery side. A general peritonitis was present without the slightest evidence of any

the introduction of air into the rectum. It is logical that a blow on the abdomen, or a muscular strain, would probably force cecal contents into the appendix. If the appendix was normal and its lumen unobstructed, it might conceivably rupture, for, as Warbasse<sup>9</sup> said, if blows can rupture a normal intestine why can they not rupture the appendix? Especially does this seem possible when one considers the small lumen of the appendix, its blunt end and its rudimentary character, and remembers that an increase in the diameter is tripled in its circumferential measurement. If the appendix was normal and did not rupture, it would empty itself and harm would not result.

If, however, due to fecal concretions, adhesions, stricture of its lumen or other disease, the appendix would be unable to empty itself, fecal stasis<sup>8</sup> would result. This condition is recognized as favorable to infection. Ludington<sup>8</sup> favored fecal stasis as the main cause of appendicitis following trauma to the abdominal wall.

Van Buren,<sup>10</sup> experimenting on dogs, found that increased intra-intestinal pressure caused pressure hemorrhage at the antimesenteric surface of the intestine. He observed the condition clinically only in cases of mechanical ileus, and reported perforation on the antimesenteric surface of the intestine, usually quite close to the point of obstruction. The necrotic area corresponds roughly to the terminal anastomotic tree of the intestinal vessels, and is evidently the result of hemorrhagic infarct of the area supplied. This necrosis is usually evident first in the submucosa and inner muscular coat, but it rapidly extends to the other coats of the intestinal wall, and perforation may occur within twenty-four hours after the discoloration due to the hemorrhagic infarct is first noticed.

Following the application of force to the external abdominal wall, it is easy to visualize a rush of cecal contents into the lumen of the appendix. This force might theoretically rupture the appendix, but this undoubtedly seldom happens. It is also easy to visualize this force as causing mucosal or mucosomuscular tears, with fecal stasis, and rapid invasion of the appendix wall by pathogenic organisms. Concretions, strictures of the lumen and adhesions would increase the chances of this occurring. From the pathologic condition of the appendixes reported here it seems probable that the rush of cecal contents jammed a concretion far down in the appendix, and that from this obstruction necrosis and perforation took place on the antimesenteric side. The concretion may be considered the obstructive lesion, and the pathologic changes may be explained according to Van Buren's observation on mechanical ileus.

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9. Warbasse, quoted by Behan: *Ann. Surg.* 85:263 (Feb.) 1927.

10. Van Buren, F. J.: *Tr. South. Surg. Soc.* 36:445, 1923.

# EMPHYEMA IN INFANTS UNDER TWO YEARS OF AGE\*

WILLIAM FRANCIS RIENHOFF, JR., M.D.

BALTIMORE

AND

WILBURT C. DAVISON, M.D.

DURHAM, N. C.

Prior to the World War, the fatality rate (mortality) of empyema in infants under 2 years of age who were treated surgically was far too high. In infants under 2 years of age, fatality rates up to 66 per cent have been reported.<sup>1</sup> The younger the patient, the higher is the rate; Holt and Howland reported that it was 71 per cent in children under 1 year of age and 59 per cent in those in their second year.<sup>2</sup> Farr and Levine found the fatality to be four times greater during the first year than in the fourth and that it steadily declined up to 6 years of age, after which the deaths occurred relatively seldom.<sup>3</sup> Wilensky reported a fatality of 48 per cent for the first year and 31 per cent during the second.<sup>4</sup> Practically the same figures have been published by Poynton and Reynolds,<sup>5</sup> Ladd and Cutler<sup>6</sup> and Bohrer,<sup>7</sup> all of whom reported in infants under 2 years of age a fatality rate of 35.4 per cent followed by a marked decrease in the frequency of deaths after the age of 2 years. However, the pediatric and surgical staffs were not proud of their results and took counsel among themselves for measures to improve them. The striking benefits which followed late operation, preceded by therapeutic aspirations and simpler methods of treatment of persons

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\* From the Departments of Surgery and Pediatrics of the Johns Hopkins University School of Medicine and Hospital and the Harriet Lane Home.

\* Read at the Fifty-Eighth Annual Meeting of the Medical Society of Virginia, Petersburg, Va., Oct. 19, 1927.

1. Thursfield, H.: The Treatment of Empyema in Infants and Young Children, *St. Bartholomew's Hosp. J.*, Nov., 1922, pp. 1-10. Holt, L. E., and Howland, J.: *The Diseases of Infancy and Childhood*, ed. 9, New York, D. Appleton & Company, 1926, pp. 442-449. Poynton, F. J., and Reynolds, F. N.: A Method for Diminishing Mortality in Empyema in Infancy and Childhood, *Lancet* 2: 1100, 1921.

2. Holt and Howland (footnote 1, second reference).

3. Farr, C. E., and Levine, M. I.: Empyema in Children, *Surg. Gynec. Obst.* 46: 79 (Jan.) 1928.

4. Wilensky: Empyema of Thorax, *Surg. Gynec. Obst.* 20: 501, 1915.

5. Poynton and Reynolds (footnote 1, third reference).

6. Ladd, W. E., and Cutler, G. D.: Empyema in Children, *Am. J. Dis. Child.* 21: 546 (June) 1921.

7. Bohrer, J. V.: Treatment of Acute Suppurative Pleurisy in Children, *Am. J. Surg.* 3: 232, 1927.

walling off process. He did not show any improvement after his operation, and died on the third day. Two concretions were found in the region of the appendix, free in the purulent material that filled the abdominal cavity.

**CASE 4.**—D. S., aged 18, who had not had any previous attacks of appendicitis, fell hard while skating, striking his buttocks. He felt pain immediately around the umbilicus and in the right lower quadrant. He felt faint and chilly, was nauseated and vomited once. Shortly after the accident, his abdominal pain lessened somewhat, but it was present constantly to the time of operation. After twelve hours, his abdominal symptoms became more marked, and they steadily increased in severity until I saw him twenty-six hours after his fall; I performed an appendectomy immediately. A general peritonitis was present, a large abscess cavity was observed in the right lower quadrant, and a concretion was found in this cavity. The appendix was  $2\frac{1}{2}$  inches (6.27 cm.) long; its wall was thickened and necrotic. Near the tip was a perforation 1 inch (2.5 cm.) long, with everted edges. This perforation was on the side opposite the mesentery. The patient recovered after the appendectomy with drainage.

#### CONCLUSIONS

1. At the time of injury all these patients were in good health.
2. A history of previous attacks of acute appendicitis could not be obtained in any case.
3. There was, in each case, a definite history of severe trauma, with immediate abdominal pain, nausea and vomiting. The symptoms were continuous up to the time of operation.
4. In each case, a perforation opposite the mesentery was found in the appendix. In each case, a concretion was recovered which presumably had perforated through the appendix. I believe that the trauma caused the concretion to impinge tightly in the lumen of the appendix resulting in an obstruction in that organ, with hemorrhagic infarction, necrosis and perforation on the antimesenteric border, bearing out the observation made by Van Buren on mechanical ileus.



We searched<sup>10</sup> all of the records of case histories of the Johns Hopkins Hospital since its opening in 1889 and of the Harriet Lane Home (the Children's Department of the Johns Hopkins Hospital) from its beginning in 1914, and were able to find reports of only eighty cases of empyema in infants under 2 years of age. The first patient was admitted to the hospital, Dec. 8, 1914, and the first operation was done, May 25, 1915. It is, of course, possible that there may have been other infants in whom empyema was diagnosed and not recorded, but it is more likely that the diagnosis of empyema in young infants in this hospital was relatively uncommon prior to 1914 and that operations for this condition in small infants were rarely performed before 1915.

Of these eighty patients, thirty-two were not operated on. In twenty of these, the diagnosis was not made until autopsy. The

*All of the Infants Two Years of Age and Under with Empyema Admitted to the Johns Hopkins Hospital from 1889 to June, 1927, Whose Records Could be Found*

Forty-eight patients who were operated on for empyema (rib resection—open thoracotomy—or the insertion of a trocar and cannula—closed thoracotomy), 19 of whom, or 39.6 per cent died.

Nine patients who had one or more thoracenteses performed (needle and syringe) and no further operation; 1 of these 9 patients recovered; 6 of them died within forty-eight hours of the diagnosis of empyema before an operation could be performed.

Three patients who were taken elsewhere for treatment after the diagnosis had been established by thoracentesis; their subsequent history is unknown.

Twenty patients in whom the diagnosis of empyema was not made until autopsy.

Total, 80 patients.

clinical diagnosis in each instance was pneumonia. Whether recovery would have been possible if the presence of empyema had been ascertained and proper treatment instituted is impossible to state. It is also unreasonable to allege that every case of empyema in infants in which the diagnosis is not made is fatal, for naturally we do not know in how many undiagnosed cases the patients recovered. However, the fact that among a total of eighty proved cases of empyema in infants under 2 years of age in this hospital, in 20 or 25 per cent of the total the diagnosis was not made until autopsy should be a warning to pediatricians to be on their guard.

There are several reasons for this failure to diagnose empyema in infants: First, the area of the chest is small, and it is often difficult to distinguish by percussion a small area of flatness from the surrounding pulmonic dulness. Secondly, most physicians hesitate to make repeated

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10. We wish to express our thanks to Miss R. Frances Riach and to Miss Laura Hodges for their assistance in locating these histories.

with empyema during the war, especially at Camp Lee, Va.,<sup>8</sup> led to the increased utilization of the closed thoracotomy or the operation<sup>9</sup> in which the trocar and cannula were used, in this hospital, and to the gradual reduction in the number of open thoracotomy or rib resections, the surgical method which has been employed almost exclusively up to 1919. Both of these operative procedures have now been used for the last nine years, and an analysis of the results has been made in order to determine whether the fatality rate had been decreased, and if not, to learn what might lead toward a reduction.

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8. Dunham, E. K., and others: Report of Empyema Commission, U. S. A.: Cases of Empyemata in Camp Lee, Va., J. A. M. A. 71: 366 (Aug. 3) 1918: 71: 443 (Aug. 10) 1918.

9. The two types of operation used in this series of cases have been the closed trocar and cannula method and the open thoracotomy or rib resection. The latter is familiar to every surgeon and need not be described here. The method in which the trocar and cannula are used is performed as follows: The skin and subcutaneous tissue over the area of most marked flatness, usually the seventh and eighth interspace between the middle and posterior axillary lines, is infiltrated with 0.5 per cent novocaine. A small incision (about 0.5 cm.) is then made in the skin and the rather blunt trocar and cannula (*B* in illustration) inserted, as shown in the accompanying illustration. After the trocar has passed the skin and subcutaneous tissue, the point is shifted as far laterally as possible and then forced through the intercostal muscles into the pleural cavity. This diagonal insertion of the trocar insures a more tightly fitting connection about the tube and thus prevents the subsequent leakage of air into the pleural cavity and also the escape of the exudate onto the wall of the chest and the formation of cellulitis. The trocar should be guarded against too deep penetration by placing the fingers on the trocar at a distance from the point approximately equal to the thickness of the wall of the chest. A rubber catheter (no. 20 or larger) clamped at the end is inserted into the side arm of the cannula (*B*) and then, as the trocar is removed, into the main tube of the cannula. The cannula is then slipped out over the catheter, leaving the latter inserted in the pleural cavity. One arm of a Y-shaped glass tube is then connected to the catheter, another arm to a 1 liter gravity flask containing warm sterile salt solution suspended 6 feet from the floor, and the third arm to a 2 liter drainage bottle placed on the floor beside the bed. The rubber tubing of the two latter connections is compressed by clamps, as shown in the illustration, but while these connections are being made salt solution is allowed to run into the Y-shaped glass tube from the gravity flask in order to expel any air in the system. The clamps on the catheter and on the connection to the gravity flask are then removed and from 25 to 50 cc. of salt solution is permitted to flow into the empyema cavity. The upper clamp is then replaced, the clamp on the connection to the collection bottle removed and the empyema cavity is thus drained. The end of the rubber tubing going to the collection bottle should always be under water to prevent the ingress of air into the system. This flushing and draining of the pleural cavity can be repeated at various intervals. During the remainder of the time the upper clamp should be in place and the lower clamp removed so that the cavity may drain continuously. Surgical solution of chlorinated soda (Dakin's solution) can advantageously be substituted for the salt solution at the end of forty-eight hours.

pneumonia and the operation, length of the postoperative stay in the hospital, nutrition, digestive condition and general physical condition of the patient, symptoms, temperature, white blood count and hemoglobin content on admission, examination of the urine, preceding infection, physical signs, location of the empyema, etiology, tuberculin reaction, preoperative and postoperative x-ray, operator, date, type and length of operation, type of pus in the empyema cavity, type of anesthetic used, pulse, respiration and temperature during and after the operation, local and general postoperative treatment, postoperative feeding, postoperative weight curve, time required for sterilization and expansion of the lungs, preoperative and postoperative complications and the cause of death in fatal cases.

#### DATA OF CASE HISTORIES

We arranged this mass of data in tables,<sup>11</sup> first finding the median (average), minimum and maximum value for each factor and then determining the effect which this factor had on the case distribution<sup>12</sup> and the fatality rate<sup>13</sup> (mortality). We found (table 1) that the cases were fairly and uniformly distributed in the various component groups and that most of the factors had more or less influence on the fatality rate, as, for example, the fatality rate in infants in the first year of life was slightly higher than that in those in their second year. The most striking effect was exerted by the following factors: the physical condition of the patient, location of the empyema, etiology, complications and the type of operation.

*Physical Condition of the Patient.*—One half of the patients were in poor physical condition. As would be expected, the case fatality rate was highest among infants in poor physical condition.

*Location of the Empyema.*—The cases were quite evenly distributed between those of empyema on the left side and those of empyema on the right. The fatality rate was highest in infants who had left sided and double empyema. That double empyema should be more fatal is to be expected but why should empyema on the left side have a fatality rate nearly twice as high as that of involvement of the right side? Can the displacement and compression of the heart with the associated cir-

11. We are indebted to Dr. Raymond Pearl for instructing us in the statistical methods necessary for the analysis of these data. For the sake of brevity, only six of the tables are included in this paper.

12. Case distribution refers to the percentage of the total number of surgically treated patients suffering from empyema that occurs in each group, i. e., in table 2, twenty-six of the total number (forty-one) of patients had pneumococcus empyema or a case distribution of 26:41, or 63.5 per cent.

13. The case fatality rate is calculated with reference to the number of patients in each group, i. e., in table 2, of the twenty-six patients who had pneumococcus empyema, eight died, or a case fatality rate of 8:26, or 30.8 per cent.

diagnostic thoracenteses. The insertion of a needle into the thoracic cavity is not entirely devoid of danger to the patient, and occasionally a serious and sometimes fatal pyopneumothorax may follow a needle puncture of the lung; in rare instances, sudden death from the so-called pleural reflex may occur. However, the case fatality rate of infants with empyema in whom the condition is undiagnosed and untreated is so much higher than it is among patients in whom needless punctures have been made for suspected empyema that Osler's admonition to a young intern should be profitably followed: "In any case of presumptive empyema, an exploring needle should be inserted in seventy times seven places before the possibility of empyema can be eliminated." The third difficulty in the diagnosis of empyema is that roentgenograms of the involved lung frequently are not of much assistance in helping one to distinguish between pneumonia and empyema, particularly if there is only a thin layer of fluid. Fluoroscopy should be more commonly used in the diagnosis of pulmonary disease in children, particularly if the presence of fluid is suspected. If one changes the infant's position on the fluoroscopic table, the level of the fluid or pus can be much more easily detected than is possible in a routine roentgenogram. Furthermore, the use of an exploring needle in the fluoroscopic room usually decreases one's failures in the diagnosis of empyema.

The remaining twelve of the thirty-two cases of empyema in infants under 2 years of age in which an operation was not performed were made up of three in which the result is unknown, for the infants were taken elsewhere for treatment after the diagnosis had been made by thoracentesis in our outpatient department, and of nine in which the treatment consisted of single or repeated aspiration of the pus in the chest with a syringe and needle. Eight of these nine infants died. These nine instances of aspiration with eight deaths, of course do not indicate that this procedure is worthless as a therapeutic measure, for six of the patients died before an operation could be performed. Thoracentesis in these cases should be classified as a diagnostic or a preoperative procedure rather than a therapeutic measure. Others who have relied solely on this form of treatment have reported good results. However, Holt and Howland reported that of 139 patients treated by aspiration alone 13 died; 101 were later operated on, and 25 were cured, 8 of them by a single aspiration.<sup>2</sup>

Our main interest lay in the forty-eight cases in which either the open thoracotomy (rib resection) or the closed thoracotomy (in which the trocar and cannula were used) had been performed. We obtained the following data from every history in which they were recorded: name, hospital number, address, age, sex, color, weight, date of admission, result, date of last observation, length of postoperative observation, duration before admission, length of the interval between the onset of

in which rib resection was done. Instead of decreasing the fatality rate in empyema in infants under 2 years of age the use of the trocar and cannula with siphon drainage had actually increased the number of deaths. This observation illustrates the advisability of analyzing hospital

TABLE 2.—*The Distribution of Cases and Deaths in Relation to the Etiology*

Etiology	Number of Patients	Case Distribution, per Cent	Number of Deaths	Case Fatality, per Cent
Pneumococcus.....	26*	63.5	8	30.8
Staphylococcus aureus.....	8†	19.5	3	37.5
B. influenzae.....	8‡	7.3	2	66.6
Streptococcus.....	4§	9.7	4	100
(Nonpneumococcus).....	(15)	(36.5)	(9)	(90)
Total.....	41‡	100	17	41.5

\* Of these, 2 were type I (no deaths); 2 were type II (both died); 1 was type III (recovered); 8 were type IV (2 deaths) and 18 were untyped (4 deaths).

† Four of these cultures contained a few pneumococci (2 type IV and 2 untyped) (2 deaths).

‡ One of these cultures contained a few pneumococci (patient died).

§ One of these cultures was *Streptococcus hemolyticus*, one *Streptococcus nonhemolyticus* and two were untyped (all died).

¶ The etiology was not recorded in 7 additional cases (2 fatal).

TABLE 3.—*Distribution of Cases and Deaths in Relation to the Presence or Absence of Complications*

Complications	Number of Patients	Case Distribution, per Cent	Number of Deaths	Case Fatality, per Cent
Absent.....	27	56.2	4	14.8
Present.....	21*	43.8	15	71.4
Total.....	48	100	19	39.6

\* Of these, 5 had septicemia, 1 septicemia and pneumococcus meningitis, 1 pneumococcus meningitis, 1 pericarditis and pyelitis, 1 myocarditis, 1 erysipelas, 1 abscess of the lungs, 1 bronchiectasis (all 12 of these died); 3 had pneumococcus peritonitis (2 died); 2 had pyopneumothorax (1 died); 2 had measles, 1 diphtheria and 1 varicella (all 4 recovered).

TABLE 4.—*Distribution of Cases and Deaths in Relation to the Type of Operation Performed*

Type of Operation	Number of Patients	Case Distribution, per Cent	Number of Deaths	Case Fatality, per Cent
Rib resection.....	24	52.2	7	29.2
Trocar and cannula.....	22	47.8	11	50
Total.....	46*	100	18	39.2

\* The type of operation was not recorded in 2 additional cases (1 fatal).

records from time to time to determine whether methods which are advocated are accomplishing their purpose. The essential difference between these two procedures is that when the trocar and cannula are used the size of the aperture for drainage is sacrificed in order to reduce the amount of operative trauma and also to prevent the leakage of air into the thoracic cavity. Apparently the reason for the lower fatality

culatory embarrassment which is usually greater in empyema on the left than that on the right be the explanation.

*Etiology* (table 2).—Similar to the series described by Holt and Howland,<sup>2</sup> nearly two thirds of the infections were due to pneumococci. Fortunately, the fatality rate in pneumococcal infections was only one half of that in infections due to other organisms. Although there were only four patients who had streptococcus empyema, so that definite conclusions cannot be made, this organism is apparently the most dangerous of all.

TABLE 1.—*Summary: The Distribution of Cases and Deaths in Relation to Various Factors*

Factor	Case Distribution	Case Fatality
Age.....	Slightly higher in infants in second year of life	Slightly higher in infants in first year of life
Sex and color.....	Highest in white males	Lowest in white males
Weight.....	Highest in infants under normal weight	Highest in those least under normal weight
Interval between onset of pneumonia and operation	No apparent relation	No apparent relation
Length of stay in hospital of patients who survived	35 days was the median (average) stay in the hospital	
Length of survival in fatal cases	.....	One half of the deaths occurred within the first four days after operation
Patient's condition.....	Highest in infants in poor condition	Highest in infants in poor condition
White blood count.....	No apparent relation	Lowest in infants with white blood counts between 20,000 and 30,000
Hemoglobin.....	Highest in infants with a low hemoglobin content	No apparent relation
Location of empyema....	No apparent relation	Higher in infants who had left sided and double empyema
Etiology.....	Highest in infants who had pneumococcus infections	Lowest in infants who had pneumococcus infections
Type of operation.....	No apparent relation	Higher in infants on whom the trocar and cannula operation or closed thoracotomy was performed
Type of pus.....	Higher in infants who had thick pus	No apparent relation
Type of anesthetic.....	No apparent relation	No apparent relation
Complications.....	Higher in infants without complications	Higher in infants who had complications

*Complications* (table 3).—The fatality rate was four times higher among the infants who developed complications than in the group who did not. Although the development of complications may have been merely an index of the lack of resistance in these infants who were ill, it is probable, as will be brought out later, that they are the most important factor in the fatality rate, and that every precaution should be taken to avoid them.

*Type of Operation* (table 4).—It was surprising to us, for we had expected quite the opposite, to find that the fatality rate among infants in whom a closed thoracotomy (in which the trocar and cannula were used) had been performed was nearly twice as high as that in the group

The resulting entrance of air into the empyema cavity did not have any ill effects of itself, because the stage of the pneumonia is not acute, and as mentioned previously, the pleural effusion develops relatively late in the disease. As the affected lung has become stabilized by adhesions, the mediastinum is more immobile. There is therefore little danger that a pneumothorax, associated with the open thoracotomy, will interfere with the expansion of the opposite and nonaffected lung. On the other hand, the maximal amount of drainage is afforded which allows complete removal not only of the pus but of the fibrinous masses. The relatively low fatality rate in this type of case, not only in adults and older children but also, as our statistics (table 5) demonstrate, in infants on whom an open thoracotomy has been performed, is sufficient proof of the efficacy of this procedure. However, the late Dr. John Howland<sup>14</sup> after having performed many autopsies on infants who succumbed to acute empyema at the Babies' Hospital in New York City, came to the conclusion that inability to expand the compressed lung seemed to be an important factor, as a certain amount of pneumothorax was always found at autopsy. Dr. Howland was at a loss to explain why the fatality in infancy was so much higher than in older children or adults, unless it was because of this pneumothorax, and he noted "that many of these children on admission are in fairly good condition and make excellent progress for a week or more after the operation. . . . Then the temperature rises, the patients lose ground rapidly and die of exhaustion during the third or fourth week." The report of the Empyema Commission of the U. S. Army in 1918<sup>8</sup> demonstrated that the acute empyemas which occurred as complications of pneumonia caused by *Streptococcus hemolyticus*, when treatment was done in the conventional manner, i.e., immediate open thoracotomy with open drainage, were attended with an average fatality of 30.2 per cent and in some districts, of 70 per cent; the highest was 84 per cent in a series of eighty-five patients. As a result of the avoidance of open drainage of the thorax and thus a concomitant pneumothorax, of operation performed at a later stage of the streptococcic pneumonia, to which the empyema was secondary, of closed thoracotomy and then a gradual decompression of the affected pleural cavity, the fatality rate dropped to less than 5 per cent.<sup>8</sup>

The reason for this lower fatality rate is that streptococcic pneumonia is of a different type than lobar pneumonia. In streptococcic pneumonia, according to MacCallum,<sup>15</sup> there is more widespread involve-

14. (Footnote 2.) Personal communication to the authors.

15. MacCallum, W. G.: The Pathology of the Pneumonia in the United States Army Camps During the Winter of 1917-1918, Rockefeller Monograph no. 10, New York, 1919.

rate in the group in which rib resection was performed is that in the latter operation adequate drainage is immediately established and maintained, while when the trocar and cannula are used occlusion of the tube is too easily possible.

## COMMENT

Versatility in the application of therapeutic measures to surgical conditions is apt to be attended with success more frequently than is the pursuance of a routine method. This is true, it would seem, of acute empyema. The type of treatment to be employed should depend not only on the age of the patient and the infecting organism but also on the type of disease to which the empyema is a sequel and the stage of the primary disease in which the empyema is recognized as a complication. These are only the more important factors which should aid in the effort to

TABLE 5.—*Percentage of Survival in Relation to the Type of Operation Performed and the Etiology, the Location of the Empyema, the Patient's Physical Condition, His Age, the Presence or Absence of Complications*

	Percentage Who Survived	Percentage with Trocar and Cannula Operation	Percentage of Those with Trocar and Cannula Operation Who Survived	Percentage of Those with Rib Resection Operation Who Survived
<i>Pneumococcus infections</i>	69	48	60	92
<i>Infections with other organisms</i>	40	53	37	43
<i>Right-sided empyema</i>	73	52	61	89
<i>Left-sided empyema</i>	54	42	40	61
<i>Good or fair condition</i>	68	48	73	67
<i>Poor</i>	52	48	27	75
<i>Under 1 year of age</i>	55	55	42	70
<i>Over 1 year of age</i>	65	42	60	71
<i>With complications</i>	29	79	18	0
<i>Without complications</i>	55	34	62	81

determine the method of treating a person with acute empyema. However, in spite of this knowledge, it is not infrequent for a report of some new method of treatment to appear which pretends to embrace the entire field of acute empyemas, without regard for more than perhaps one important factor. New methods are, of course, always to be welcomed, but it seems to us that they should be carefully assigned to the type of case which will receive the maximum benefit from their application.

Before the World War, the type of acute empyema most often noted was that following lobar pneumonia and was caused by the pneumococcus. The pleural effusion in those cases occurs relatively late in the disease process and the involved lung is more or less attached to the wall of the chest by fibrinous adhesions. Thus the thoracic pleura and at the same time the mediastinum are somewhat stabilized. The pneumococcus pus is thick and contains many fibrinous masses of considerable size. In this type of case the open thoracotomy, either a partial rib resection or an intercostal incision and drainage, proved most efficacious.



there are relatively few, if any, adhesions between the lung and the thoracic wall to stabilize the mediastinum. In other words, the open thoracotomy is satisfactory in the treatment of adults with an acute empyema of pneumococcal origin, but in the patients with acute empyemas associated with a streptococcic pneumonia the closed method of thoracotomy is far superior. The determination in adults of at least the etiology and the type of pneumonia should dictate the choice of thoracotomy to be performed.

The results of our study in these cases of acute empyemas in infants under 2 years of age, however, would seem to demonstrate that better results can be obtained by the use of one operation, the open thoracotomy, in all cases. It is evident from our own statistics and from those previously quoted that the resistance and margin of safety in infants under 2 years of age suffering from acute empyema is slight. It would seem to us that the best treatment is immediate and adequate drainage. If the relationship of all of the factors which affect the fatality rate is considered in connection with the type of operation performed (table 5), it is apparent that open thoracotomy (rib resection) offers an infant a much better chance of recovery in every type of case, except possibly in those who are in good or fair condition and in those who develop complications. However, in those patients who are in good or fair condition, the fatality rate is practically the same with each type of operation (table 5). With regard to patients with complications, it is true that all three of the patients who developed complications after the rib re-section died, while two of the eleven who developed complications after the use of the trocar and cannula survived. However, as nearly as we could judge, the great majority of the complications were recognized some time after the operation had been performed, so we are inclined to believe that they resulted from inadequate drainage. As may be seen in table 6, the development of complications is probably the most important factor in case fatality; there is little difference in the chances of survival if complications are absent. Therefore, since complications occur four times as frequently after the closed thoracotomy (trocar and cannula) than after the rib resection, it seems obvious that the latter operation is preferable in all cases.

The open thoracotomy (rib resection) is especially desirable if the empyema is due to the pneumococcus, for the large masses of fibrin do not interfere with the drainage of the cavity as they do with the closed method. Ninety-two per cent of the infants who had pneumococcal infection and on whom rib resection was performed survived in contrast to 50 per cent on whom closed thoracotomy was performed (table 5). In empyema due to other organisms, the effect of the type of operation was unimportant. In other words, pneumococcic infection and rib resection are two favorable factors in producing a low fatality rate. Obviously



Thus, it seems to us that this series of cases of acute empyema in infants under 2 years of age may be considered a parallel series in which two types of thoracotomy were employed, i. e., the open and the closed method.

#### CONCLUSIONS

An analysis has been made, in relation to several factors, of the distribution of cases and deaths in a series of forty-eight cases of empyema in infants under 2 years of age, in whom the condition was treated surgically. Five of these factors have a striking effect on the fatality rate, i. e., the fatality rate was highest among infants in poor physical condition, those who had left sided or double empyema, those who had nonpneumococcal infections, those who developed complications and those in whom operation was performed by means of the closed thoracotomy or the trocar and cannula method. It is, of course, obvious that the patient's physical condition and the presence of complications should play rôles in the fatality rate, but, as far as we know, it has not been demonstrated in young infants that the location of the empyema, the etiology and the type of operation were as important as our tables would seem to indicate. A knowledge of the effect of four of the five factors is merely an aid to prognosis, but it seems to us that the higher fatality rate among infants in whom the closed thoracotomy (trocar and cannula) was performed is of therapeutic significance and should, if other studies confirm our figures, lead to the abandonment of that operation in the treatment of infants under 2 years of age with empyema.

It is our impression that in infants open thoracotomy (rib resection) is on the whole a more satisfactory procedure than closed thoracotomy (in which the trocar and cannula were used) mainly because an immediate, uninterrupted free drainage of the affected pleural cavity is accomplished. We feel that the slight blocking which often occurred in the closed thoracotomy was in all probability mainly responsible for the marked increase in complications associated with this procedure. Owing to the fact that a lateral intercostal incision is so frequently associated with a pinching and occlusion of the rubber drainage tube, the partial rib resection is the method of open thoracotomy to be preferred. A partial pneumothorax resulting from the open thoracotomy is apparently less dangerous than is the inadequate drainage associated with the closed thoracotomy.

the type of infection is beyond human control but, fortunately, pneumococci are responsible for about two thirds of the cases. In the forty cases in which the etiology and the type of operation were recorded, twenty-five were due to pneumococci and fifteen were due to other organisms. If the rib resection had been done in all instances, only two deaths would have been expected among those in whom the infection was of the pneumococcic type (8 per cent) and nine among the remainder (57 per cent), making a total fatality rate of 27 per cent, which would be a marked improvement over the present rate of 40 per cent.

The younger the patient and the poorer his condition, the more important it is to establish free drainage immediately, for, as shown in table 5, the percentage of survival among infants under 1 year of age

TABLE 6.—*Percentage of Survival in Relation to the Presence or Absence of Complications and the Type of Operation Performed, the Etiology, the Location of the Empyema, the Patient's Physical Condition*

	Percentage Who Survived	Percentage with Complications	Percentage of Those with Complications Who Survived	Percentage of Those without Complications Who Survived
Trocar and cannula	50	50	18	82
Rib resection	71	12	0	81
Pneumococcus infections	69	35	33	88
Infections with other organisms	40	53	12	72
Right-sided empyema	73	41	56	85
Left-sided empyema	54	37	11	80
Good or fair condition	68	20	43	77
Poor condition	52	56	23	91

and among those in poor physical condition was respectively two and three times higher when the rib resection was performed than it was after the closed thoracotomy. Yet it was for these younger patients and for those in poor physical condition that the operation in which the trocar and cannula were used was especially recommended!

It is our opinion, that there is little difference in the shock to the infant resulting from the closed or open thoracotomy. Equal amounts of local anesthetic have been used in both types of operation and approximately the same amount of time has been consumed by the two procedures, so that there is little difference between the actual performance of them that would tend to recommend one in preference to the other. Another interesting fact brought out by this study is that the patients were operated on by different surgeons in this hospital from 1915 until 1928, and the case fatality rate was about the same for all. Each operator's technic for the closed and open thoracotomy, together with the preoperative and postoperative care, was almost identical, so that the operation and the postoperative care can be considered almost a constant

cases of tumors of the tendon sheaths and stated the results of a review of various groups of similar tumors reported in the literature. His summary follows:

1. Primary tumors of tendons are very rare. The commonest of them are the sarcomata.

2. Primary tumors of tendon sheaths are more frequent. The commonest among them are the giant-myelomata (granulomata).

3. The giant-celled myeloma seems to be caused by some injury or irritation. It is an inflammatory granuloma, and should therefore, be excluded from the group of neoplasms and included in that of inflammatory disease.

4. The following classification and terminology of the tumors of tendons and tendon sheaths should be adopted: *A. Neoplasms: I. Neoplasms of tendons; (1) Benign neoplasms: fibroma, osteoma, chondroma; (2) Malignant neoplasms: sarcoma. II. Neoplasms of tendon sheaths; (1) Benign neoplasms: fibroma, lipoma, chondroma, angioma; (2) Malignant neoplasms: sarcoma; (3) Mixed neoplasms. B. Inflammatory and other tumors: tendovaginitis, tuberculosa: granuloma (the former, myeloma), ganglion, etc.*

5. The differential diagnosis between the tumors of tendon sheaths and inflammatory diseases, especially tendovaginitis tuberculosa granulosa, is difficult.

*Endothelial Myeloma (Ewing's Tumor).*—Sycamore and Holmes<sup>36</sup> reviewed the subject of endothelial myeloma, finding the incidence of this neoplasm probably as about 10 per cent of tumors of the bones. They concluded from their studies that the condition should be sharply differentiated from angio-endothelial and from osteogenic sarcoma and that it should be possible to recognize the tumor in spite of the fact that in their own experience the diagnosis has been more often missed than made. The tumor responds strikingly to roentgen-ray or radium therapy, but the prognosis is poor because of the frequency of metastasis.

*Tumors of the Cervical Spine.*—Camurati<sup>37</sup> collected reports of eighteen cases of primary giant cell tumors of the cervical spine. To these he added one case report from the Anatomical Museum and Clinical Archives of the Rizzoli Institute. Judging from the diverse opinions of many authorities, he believed that it is impossible to establish whether the nature of the process is neoplastic or an inflammatory reaction to agents of varied nature (trauma, toxins, etc.). Some authors believe that following hemorrhage in the confines of the osseous medulla, the tissues destined to form the medulla itself proliferate and form a true cellular zone in the hemorrhagic field. Thus there may be formed a fibrous tissue to surround it or invade it, transforming the coagulum into a cicatrix. In other cases the tissue that is formed subsequent to a hemorrhage from trauma may continue to grow until a tissue results that is similar to that of tumors with giant cells. This granular tissue

36. Sycamore, Leslie K., and Holmes, George W.: *Am. J. Roentgenol.* 18:223 (Sept.) 1927.

37. Camurati, M.: *Chir. d. org. di movimento* 6:581 (Nov.) 1927.

# THIRTY-SIXTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY \*

PHILIP D. WILSON, M.D.

LLOYD T. BROWN, M.D.

M. N. SMITH-PETERSEN, M.D.

RALPH GHORMLEY, M.D.

AND

MURRAY S. DANFORTH, M.D.

BOSTON

AND

HERMAN C. BUCHOLZ, M.D.

HALLE, GERMANY

(Concluded from page 534)

## TUMORS

*Synoviatoma*.—Under the name of synoviatoma, Smith<sup>34</sup> reported a group of three unusual tumors which appeared to originate from synovial membrane or similar tissue. In the first patient the tumor arose in the fascia in Hunter's canal, and the patient died at the end of six months supposedly from pulmonary metastases. Microscopically, the tumor was composed of anastomosing clefts lined by low cuboidal epithelium and separated by cords of spindle shaped cells. The second patient was a Jewess, aged 24, with a tumor extending down the thigh under Poupart's ligament. She died at the end of three years of pulmonary metastases. The third patient was a man of 35, with a tumor on the inner side of the knee. Death resulted at the end of two and one-half years, again from pulmonary metastases. The tumors in these cases were similar to that in the first. According to the author, this type of tumor may arise from the synovial membrane of the cavity of the joint itself, from the synovial membrane of overlying bursae, from fascial aponeurosis and from tendons and tendon sheaths. Two types of cells can be differentiated, the synovial lining type and the stroma type.

*Tumors of Tendon Sheaths*.—From the surgical clinic of the John Casimir University of Dwów, Poland, Janik<sup>35</sup> reported details of four

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\* This Report of Progress is based on a review of 258 articles selected from 419 titles dealing with orthopedic surgery appearing in medical literature between Sept. 24, 1927, and Feb. 25, 1928. Only those papers that seem to represent progress have been selected for note and comment.

34. Smith, L. W.: Am. J. Path. 3:355 (July) 1927.

35. Janik, Alfred: Ann. Surg. 85:897 (June) 1927.

and some degree of deformity. Only two patients were found who were entirely free from symptoms and who showed a useful range of motion.

*Comparative Results of Operative and Nonoperative Treatment of Pott's Disease in Children.*—After a trial of nonoperative and operative methods in the treatment of Pott's disease in children, Kidner and Muro<sup>40</sup> concluded that operation ought not to be performed except in selected cases and that the best treatment is absolute recumbency on a Bradford frame, under favorable environment until bony union of the diseased vertebrae is clearly demonstrable by roentgen-ray examination. The authors divided a series of fourteen cases into pairs and performed fusion operations in the alternate cases and treated the other patients without operation. From the observation of these patients, they concluded that cure depends on prolonged recumbent treatment, that cure in the patients operated on requires as long a period of time as in the patients not operated on and that the patients who are treated without operation preserve greater flexibility of the spine.

*Tuberculosis of the Knee in the Adult.*—Henderson and Fortin<sup>41</sup> studied the end-results of 211 adult patients with tuberculosis of the knee joint who were treated by resection at the Mayo Clinic. The diagnosis of tuberculosis was proved in all cases. The signs and symptoms of chief importance and the ratio in which they were present were as follows: pain, 99 per cent; stiffness, 100 per cent; limp, 99 per cent; swelling, 97 per cent, and local heat, 53 per cent. As for roentgen-ray examination, the authors stated that they do not believe that there is a typical picture for tuberculosis of the knee. Evidence of involvement of the bone was found in all but 9.87 per cent. The "bone abscesses" were usually found in the inner condyle of the femur or in the inner tuberosity of the tibia. A method of resection developed by the authors was employed in all cases. This consists of an excision of the surfaces of the joints of the tibia and femur, together with an excision of the synovia and patella. A graft consisting of a layer of the cancellous bone is laid along the anterior surface of the joined bone ends, under "leaves" of bone lifted from the front of the tibia and femur. Two wire nails are driven up through the tibia into the femur to hold the ends in apposition. The leg is then fixed in a plaster casing extending to the groin. In 194 patients who were followed, operative mortality did not occur. Two patients died of tuberculous meningitis within one year, and 8.7 per cent died within four years. Amputation became necessary later in 2.5 per cent. Nonunion resulted in 11.3 per cent, but of these patients four later obtained fusion by bone grafting operations. Dis-

40. Kidner, F. C., and Muro, Felipe: J. Bone & Joint Surg. 9:649 (Oct.) 1927.

41. Henderson, M. S., and Fortin, Harry J.: J. Bone & Joint Surg. 9:700 (Oct.) 1927.

containing giant cells is found sometimes in pseudarthroses, in formation of callus and sometimes in Köhler's disease. Such tissues can be histologically similar to a tumor with giant cells, while biologically they must be considered as a chronic process of repair.

*Tumors of Cauda Equina and Spinal Cord.*—Bennett<sup>38</sup> reported four cases of tumors of the spinal cord and cauda equina, in each of which the symptoms suggested osseous, muscular and ligamentous disturbances rather than pathologic changes in the nervous system. The tumors were revealed either at operation or at autopsy. The most prominent symptoms in these cases and the ones which the author believes point strongly to this condition are: (1) variable pain in the spine and nerve roots; (2) extreme spasm of the erector spinal muscles followed by lateral deformity of the spine, and (3) extreme bilateral spasm of the hamstring group. All these signs appeared long before any motor or sensory changes occurred.

[Ed. NOTE.—The significance of Bennett's article is that the symptoms of tumor of the spinal cord or cauda equina may, at least in the early stage, be indistinguishable from those of ordinary back strain. When the nervous system is examined, however, signs will usually be found pointing to the true nature of the lesion. Numerous instances are on record of patients with such tumors being treated for back strain over considerable intervals of time before the correct diagnosis was made. The only method by which the orthopedic surgeon may avoid such errors is to examine the nervous system in all patients with pain in the back.]

#### TUBERCULOSIS

*Results of Treatment of Tuberculosis of the Hip.*—Smith and Watters<sup>39</sup> recently completed a study of 208 patients who were treated for tuberculosis of the hip at the Country Branch of the New York Orthopaedic Dispensary and Hospital. Only nonoperative methods of treatment were employed. In this group, the diagnosis was found to have been wrong in forty-six, or 22 per cent of the patients. The only way to eliminate such errors is by aspiration or exploratory operation to obtain material for pathologic investigation and inoculation into guinea-pigs. Of 150 patients who were followed for three years or more, thirty-six, or 24 per cent, died, the majority of tuberculosis. In seventy-one patients, or 47 per cent, the tuberculous process in the hip was found to be still active. In forty-one patients, or 27 per cent, the process was found to be quiescent, with little if any motion in the hip

38. Bennett, George E.: Tumors of Cauda Equina and Spinal Cord, J. A. M. A. 89:1480 (Oct. 29) 1927.

39. Smith, Alan DeForest, and Watters, W. H.: Tuberculosis of Hip, J. A. M. A. 90:189 (Jan. 21) 1928.



*Synovial Tuberculosis.*—Peabody<sup>45</sup> described five patients with tuberculous lesions of the joints which seemingly involved only the synovial structures, and expressed the opinion that they establish the fact that tuberculosis may exist solely as a lesion of the synovia. His observations are summarized as follows: Five patients suffering from a chronic disorder of the joints of from two to seven years' duration presented physical manifestations inconsistent with those commonly looked for in established tuberculosis of the joints, and roentgen-ray examination was negative for destruction or absorption of bone. Operation was performed in all of the cases, and the pathologic condition found was that of long standing tuberculosis distributed throughout the synovial membrane and unaccompanied by any lesion of the bone. Four of the patients were adults between the ages of 23 and 31, in excellent general health and free from constitutional stigmas of tuberculosis. In none did a preoperative diagnosis of tuberculosis of the joints seem to have clinical support.

[ED. NOTE.—It seems to us that the evidence adduced by the author is insufficient to justify his conclusions.]

#### PYOGENIC INFECTIONS

*Pathogenesis and Treatment of Acute Epiphysitis.*—Wilensky<sup>46</sup> expressed the belief that in acute epiphysitis the dominant characteristics of the pathologic picture are (1) a thrombo-arteritis or thrombo-phlebitis and (2) a necrosis of bone and cartilage cells consequent to the disturbance of circulation produced by the plugging of the vessels. Clinically, he divided the cases of acute epiphysitis into three groups: 1. In the first variety, a focus is present in one of the epiphyses with well marked local signs and symptoms, but without any clinical signs of a general blood infection. 2. In the second variety, a well marked focus is present in one of the epiphyses with abundant local signs and symptoms and, in addition, there are clinical indications of a bacteremia as evidenced by the general signs and symptoms and by the demonstration of living bacteria in the blood stream. 3. In the third variety the clinical picture is that of a profound general infection with a marked toxemia. A local focus is either not demonstrable at all because of the paucity of local signs and symptoms or because the latter is concealed by the profound intoxication, or, if present, the local lesion is easily recognized as not being of any consequence in the total clinical picture. Blood cultures are of assistance in determining the severity of the lesion and in suggesting the appropriate treatment. In the absence of a demonstrable bacteremia, conservative treatment is desirable, other things

45. Peabody, Charles E.: Ann. Surg. 86:92 (July) 1927.

46. Wilensky, Abraham O.: Ann. Surg. 86:105 (July) 1927.

charging sinuses still remain in 2.06 per cent of the patients. In 23.7 per cent tenderness was present, usually along the scar. Primary bony union was obtained in 88.3 per cent. The authors state that with their present technic (graft) they expect to obtain firm union in from five to eight months.

*Quantitative Tuberculin Reaction.*—After a discussion of allergy, on which the tuberculin reaction is based, Atsatt<sup>42</sup> stated that by means of a special quantitative examination it is possible to determine approximately the activity of tuberculous foci. Using the same lot of Saranac tuberculin throughout the series, he injected intradermally 1 cc. of old tuberculin in dilutions of 1:1,000, 1:2,500, 1:5,000, 1:7,500 and 1:10,000. Because of the degree of the skin reaction or of the fluctuation of allergy in direct proportion to the activity of the disease, the author found that by establishing a critical threshold (in this series, a dilution of 1:7,500), active tuberculosis could be diagnosed with a fair degree of certainty. The test was employed in patients with tuberculous and nontuberculous lesions of the bones and joints, on whom operation was later performed and the opportunity thus afforded of verifying the tests by examination of pathologic material.

[ED. NOTE.—We have had the opportunity of seeing Atsatt's quantitative tuberculin reaction employed at first hand in a series of more than 100 cases. We are convinced that it is a more reliable test of tuberculosis of the bones and joints than the ordinary tuberculin skin test.]

*Effect of Rachitogenic Diet on Experimental Tuberculosis.*—Grant, Suyenaga and Stegeman<sup>43</sup> succeeded in demonstrating experimentally that white rats can be made susceptible to inoculation of tuberculosis by decreasing the calcium and vitamin D content of the diet. The animals developed tuberculosis of the lungs, which was proved by pathologic examination and inoculation into guinea-pigs. Control rats which received an adequate diet before and after subcutaneous inoculation with tubercle bacilli remained immune even after relatively large doses.

*Rice Bodies in Tuberculosis.*—Rogers<sup>44</sup> reported the case of a patient with tuberculous tenosynovitis who showed the presence of numerous rice bodies. The diagnosis was proved by the examination of material removed at operation. The process of formation of the rice bodies could be followed in the tissues, and from a study of the pathologic material the author stated that it was apparent that the rice bodies represent the centers of tubercles.

42. Atsatt, Rodney F.: J. Bone & Joint Surg. 9:657 (Oct.) 1927.

43. Grant, A. H.; Suyenaga, B., and Stegeman, D. E.: Ann. Rev. Tuberc. 16: 628 (Nov.) 1927.

44. Rogers, Mark H.: J. Bone & Joint Surg. 9:636 (Oct.) 1927.

munities should encourage public health nurses to teach precautions in the home. Expert diagnosticians should be employed during epidemics, and cases should be promptly reported.

#### BOOK REVIEW

*Poliomyelitis.*—MacAusland<sup>49</sup> has written probably the best text-book on poliomyelitis that is available at present. It brings to date the knowledge on history, epidemiology, etiology, pathology and treatment of the disease in the acute stage. The chapter on the epidemiology is particularly valuable, because of the extensive collection of epidemics described. There is some inconsistency in respect to the length of time during which improvement may be expected to take place. In one place six months is given as the maximum time, while elsewhere, it is stated that operation should not be performed until after the lapse of two years because of the improvement that may take place. The surgical treatment is discussed at length, with good operative illustrations. The author is an ardent advocate of astragalectomy and reports 400 cases, with twelve failures, as against six cases of stabilization of the foot by subastragalar arthrodesis. Also, more space appears to be devoted to tenodesis and Whitman's loop operations than the value of these procedures seems to justify. The author has attempted to standardize the surgical treatment, always a difficult thing in as variable a condition as poliomyelitis, and the reader is left in considerable doubt as to what procedure to follow in the various conditions.

#### VASCULAR DISEASES

*Spontaneous Gangrene.*—Discussing the pathology of the different types of gangrene of the extremities, Lewis<sup>50</sup> divided these conditions into: (1) arteriosclerotic gangrene; (2) arteriosclerotic gangrene with glycosuria (diabetic gangrene), and (3) thrombo-angiitis. In all of these conditions, the development of a collateral circulation is of prime importance. Lewis recommended ligation of the femoral artery, which he has performed in seven cases. One death, two cases in which amputations were performed later and four in which improvement occurred were noted in this series.

*Erroneous Diagnosis.*—Allen and Brown<sup>51</sup> pointed out that the diagnosis of vascular diseases is comparatively easy in 90 per cent of the cases, but that in the remaining 10 per cent there is a high incidence of error. They reported in detail the conditions found microscopically in tissues obtained in eight cases which had been diagnosed as Raynaud's disease but which on pathologic investigation were shown to be cases

49. MacAusland, W. R.: *Poliomyelitis*, Philadelphia, Lea & Febiger, 1927.

50. Lewis, Dean: *Canad. M. A. J.* 17:1125 (Oct.) 1927.

51. Allen, E. V., and Brown, G. E.: *Am. J. M. Sc.* 174:319 (Sept.) 1927.

being equal, and later a minor operation alone may be indicated. In the presence of a demonstrable bacteremia and a definite focus, elimination of the focus is indicated, as little damage as possible being done. In the fulminating types, even with a demonstrable focus, the prognosis is always grave, with little help from operative procedures.

#### POLIOMYELITIS

*Experimental Immunization.*—The results of experiments on monkeys to produce immunity to poliomyelitis have been reported by Aycock and Kagan.<sup>47</sup> Pointing out that one attack of the disease confers lasting immunity and that the blood serum of convalescent patients is virucidal, the authors stated that attempts so far to increase the penetration of the serum in the central nervous system and to develop a hyperimmune serum have been unsuccessful. Killed virus does not have immunizing power. Experiments have been made with an attenuated virus which had been treated with phenol, 0.25 per cent to 1 per cent and diluted with glycerin, 5 to 50 per cent. The results were variable, and a vaccine which was effective in producing immunity was still virulent enough to kill from one third to one half of the animals used. With subcutaneous inoculation, less than one half of the monkeys developed the disease. Of two animals inoculated by scarification, one developed the disease and the other died of tuberculosis. Repeated intracranial injection produced infection in a small number of monkeys and prolonged the incubation time. Of twelve monkeys so treated, one developed the disease, two resisted three intercerebral inoculations, two resisted two such inoculations, three resisted one inoculation, and one showed prolongation of the incubation period.

*Control of Infection.*—Discussing the control of poliomyelitis, Ebright<sup>48</sup> stated that the disease is spread chiefly by direct contact with people who harbor the virus in the nose and mouth. These people may be developing the infection or they may be carriers or convalescents. Infection takes place by the mouth, nose, conjunctiva of the eye and the tear duct and stomach. Prevention of spread of the infection is to be accomplished by adequate bedside precautions. There is no evidence that regulations against the congregation of people has any influence. All discharges from the nose, throat and bowel should be de-infected. Caretakers, nurses and physicians should guard against infection from contamination with discharges or secretions on hands and clothing. Patients should be thoroughly bathed, the hair included, on the preceding day of isolation, which should last for from two to three weeks.

<sup>47</sup> Aycock, L., and Kagan, J. R.: *J Immunol* 14:25 (1927).

<sup>48</sup> Ebright, G. E.: *California & West Med* 27:374 (1927).

the onset of trophic changes, "rest pain" occurs in contradistinction to claudication or "exercise pain." The disease is usually bilateral. The arteriosclerotic type of disease is well understood, but the differential diagnosis in men between the ages of 45 and 55 is sometimes difficult. In discussing the treatment, the authors mentioned various prophylactic and reassuring measures. In Raynaud's disease of the lower extremities, lumbar sympathetic ganglionectomy is said to be curative. A useful table for differential diagnosis is included.

*Collateral Circulation.*—Bernheim and Sachs<sup>53</sup> showed that in obstructive vascular disease of the extremities, such as arteriosclerosis and thrombo-angiitis obliterans, there is a definite increase in the number and size of the blood vessels of the sciatic nerve, both in the perineural tissue and within the fasciculi as well. These symptoms are constant. This increased vascularization accounts for the survival of certain limbs long after their main blood vessels have become totally occluded. Moreover, whatever the degree of the obstructive process in the main blood channels, the sciatic vessels do not appear to be similarly involved other than by some thickening of their walls and a certain amount of calcification. Thrombosis of the sciatic vessels has not been observed in the author's experience.

*Ramisection.*—Discussing the surgical treatment of Raynaud's disease and similar conditions, Royle<sup>54</sup> pointed out that with the adoption by Lerche of ramisection, practically the only line adopted is now by means of ramisection or ganglionectomy of the sympathetic nervous system. The surface temperature is thereby increased from 2 to 7 degrees and the heat production from 200 to 900 per cent. Since the vasoconstrictor fibers reach the segmental nerves by the gray rami, it is only necessary to cut these and not to remove the whole abdominal sympathetic trunk. Of eight patients on whom ramisection was performed by the author, four with thrombo-angiitis had only temporary relief from pain but showed more or less permanent improvement in the condition of the limb. In the patients with Raynaud's disease the results were much more satisfactory, and three out of four were completely relieved. The fourth patient had involvement of the upper limb, while in all the others the lower was involved.

#### DISTURBANCES OF THE NERVOUS SYSTEM

*Pathology of Charcot Joints.*—From a study of the pathologic changes in Charcot's joint, Potts<sup>55</sup> pointed out that neuro-arthropathy may affect any joint in the body. Two conditions must obtain: a change

53. Bernheim, B. M., and Sachs, L.: *Ann. Surg.* 86:417 (Sept.) 1927.

54. Royle, N. D.: *M. J. Australia* (supp. 11), Nov. 5, 1927, p. 341.

55. Potts, W. J.: *Ann. Surg.* 86:596 (Oct.) 1927.

of obliterative vascular disease. They stated that a complete obliteration of the palpable vessels is not essential for a diagnosis. In approximately 5 per cent of patients with thrombo-angiitis obliterans the pulsations in the dorsalis pedis and posterior tibial arteries were normal. In these cases, the occluding vascular lesion involved the digital or interosseous arteries.

**Diagnosis.**—The accompanying table shows the classification of vascular diseases suggested by Brown and Henderson.<sup>52</sup>

The basic disturbance is similar in all forms of vasospastic disease, i.e., Raynaud's disease, acrocyanosis, etc. The essential points in the diagnosis of functional disorders are: (1) open palpable arteries with

*Classification of Vascular Diseases (Brown and Henderson)*

Functional or vasomotor types	Local distribution	Vasoconstricting types	<ol style="list-style-type: none"> <li>1. Multiple phase color reaction; Raynaud's disease</li> <li>2. One phase color reaction-acrocyanosis; dead finger; local syncope</li> </ol>
		Vasodilating types	Erythromelalgia
	General distribution	Vasoconstricting types	Primary or essential hypertension, early stages
		Vasodilating types	Primary or essential hypotension
Organic types	Local Distribution	<ol style="list-style-type: none"> <li>1. Arteriosclerosis with or without thrombosis; diabetic gangrene</li> <li>2. Thrombo-angiitis obliterans</li> <li>3. Simple thrombosis or embolism</li> </ol>	
		4. Arteritis of known infectious origin (rheumatic-syphilitic)	
		5. Aneurysm with or without thrombosis	
	General distribution	Arteriosclerosis <ol style="list-style-type: none"> <li>1. Primary</li> <li>2. Secondary to hypertension</li> </ol>	

pulsation; (2) intermittent changes in color and temperature; (3) distribution usually in all four extremities. Erythromelalgia (Weir Mitchell) is functional and nonprogressive and is relieved by cold and elevation of position. These changes may to a less degree accompany the organic types of disease. Thrombo-angiitis obliterans as a disease entity is discussed. The authors pointed out that Rabinowitz isolated an organism from patients and succeeded in producing vascular disease in rabbit. Tobacco, race, age, sex (male) and exposure to cold are considered as contributing factors. Fifty-one per cent of the authors' patients showed claudication as an initial symptom (claudication after exertion). With

52. Brown, George E., and Henderson, M. S.: *J. Bone & Joint Surg.* 9:117 (Oct.) 1927.

operation, and there were fibrous bands which bound the nerves together. Following the operation, the vasomotor disturbances immediately disappeared, and active motion soon returned in the paralyzed dorsiflexor muscles of the foot.

[ED. NOTE.—Generalization cannot be made from the report of one case, but this article seemed to be of more than casual interest as affording a contrast to the usual pessimistic reports of the results of laminectomy in patients with similar conditions.]

*End-Results of Ramisection in Spastic Paralysis.*—By an ingenious set of graphic records of the gaits of patients with spastic paralysis, Stewart<sup>58</sup> was able to demonstrate improvement in all of twenty-seven patients subjected to the operation of sympathetic ramisection. Rigidity was reduced, coordination improved and equilibration made better. A direct effect in relieving muscular weakness was not noted.

#### MISCELLANEOUS

*Development of Bone in Diabetic Children.*—Roentgenograms of the skeleton in sixty-eight children under the age of 15 years with diabetes mellitus have been reviewed by Morrison and Bogan.<sup>59</sup> It was found that the epiphyseal development and growth of the shaft was in advance of the chronologic age in children with diabetes of recent onset. The development of bone was below the chronologic age in children with diabetes of long standing. Narrowness of the shaft and thinness of the cortex characterized long standing diabetes. Atrophy of the bone was found to occur in a certain number of children who developed diabetes before the age of 9 years.

*Physiology of Bone in Relation to Diseases of the Bone.*—Discussing the physiology of bone, Eising<sup>60</sup> said that the old idea that growth of bone tissue is a product of osteoblastic or osteoclastic activity must account not only for normal bone production but for the aberrations of the function presented in disease, including the reactions to bacterial or other invasions and tumors. He expressed the opinion that one should accept as a first premise the conception that the vital substance of bone is the collagenous intercellular material. The problem then at once falls within the domain of the chemistry of colloids. Preosseous tissue is devoid of blood vessels to such a degree that it forces the inference that the salts of lime, namely, calcium phosphate and calcium carbonate, must be an inherent part of the collagenous matrix. If one believes that the intercellular substance of bone contains in its substance the specific elements of bone, it becomes easy to conceive how by biologic activity

58. Stewart, Steele F.: *J. Bone & Joint Surg.* 9:742 (Oct.) 1927.

59. Morrison, L. B., and Bogan, I. K.: *Am. J. M. Sc.* 174:313 (Sept.) 1927.

60. Eising, E. H.: *Am. J. Surg.* 3:367 (Oct.) 1927.

in the sensory nerves and trauma to the joint. As long as the existence of trophic nerves is unproved, there is no reason to believe that this condition results from anything but the destruction that follows in a joint which lacks its protective muscular mechanism. When the bones are deprived of the accurate weight distributing power of the muscles and of the stabilizing protection afforded by an intact reflex nervous mechanism, minor stresses are bound to produce damage. So-called spontaneous fractures in tabetic patients commonly occur for the same reason. According to this hypothesis, neuropathic joints are simply variable pictures of destruction and erosion and of nature's attempt to stop the damage by sclerosis and to repair the damage by building up new bone. The bizarre pictures are the result of the excessive rapidity of both processes.

*Brachial Plexus Paralysis.*—According to Giliberti,<sup>56</sup> brachial plexus paralysis forms the second largest group of birth palsies. It occurs more frequently after births in which artificial aid is required. The cause is pressure or traction on the brachial plexus. The nerve fibers and bundles may be torn at any point. The Duchenne-Erb or upper arm type of paralysis is the most common and has the best prognosis. The Klumpke-Dejerine or lower arm type is often the residual of a combination type. In this type, sensory symptoms are usually present. The prognosis is less favorable in brachial paralysis than in ordinary injuries of the peripheral nerves. There is a danger in long existent cases that habit palsy may replace organic lesions. Treatment consists in immediate immobilization in abduction, with the forearm in full supination. If regeneration is not evident after physiotherapy has been tried for one year, then resort should be had to neurosurgery. Contractures are best overcome by methods of gradual correction.

[ED. NOTE.—If operation on the plexus is to accomplish the most, it must be performed as soon after injury as possible. Obstetric paralysis is likely to cause such severe crippling in adult life that every emphasis should be placed on early diagnosis and immediate surgical treatment. We do not agree with Giliberti that one should wait a year before resorting to operative treatment. Orthopedic treatment is important and should not be neglected, but it cannot restore severed nerves or prevent cicatricial contraction about the plexus.]

*Spontaneous Recovery of Deformity of the Foot Following Laminectomy for Spina Bifida Occulta.*—Kochs<sup>57</sup> reported the case of a patient with increasing paralytic equinus deformity of the foot, who was completely relieved by laminectomy for spina bifida occulta. A piece of bone which appeared to press on the cauda equina was found.

56. Giliberti, V.: *J. Nerv. & Ment. Dis.* 66:449 (1928).

57. Kochs, J.: *München med. Wochenschr.* 74:1877, 1927.



*End-Results and Follow-Up in Orthopedic Surgery.*—Rogers<sup>64</sup> devised a system by means of which orthopedic patients at the Massachusetts General Hospital, could be followed and the end-results studied; this system has functioned with a high degree of success during a period of three years. The clinics in which the end-results were studied one year, two years and three years after operation have been well attended; the proportion of patients reporting, including many who lived at a distance, has been nearly 80 per cent. The author described the system in detail and presented illustrations of the various forms and tables showing the results obtained. The system promotes greater cooperation between the patient and the orthopedic surgeon in the after-treatment in operative cases, and hence insures better results.

[ED. NOTE.—There is a great need in orthopedic surgery for precise knowledge as to the results of the various operative procedures. Facts must replace impressions to as large an extent as possible. The end-result clinic is the mechanism by which such facts are to be obtained. Having observed the working of Rogers' end-result system at first hand, we take the liberty of expressing the opinion that it is admirably devised to accomplish its purpose.]

*Painful Shoulder.*—After a review of 450 roentgenograms, which had been made because of a complaint of pain in the shoulder, and ascertaining that the symptoms were negative in 300, King and Holmes<sup>65</sup> were led to make a clinical study from which they drew the following conclusions: The shoulder joint is dependent for its strength on the tone of the muscles which have their insertion in the capsule. Atrophy of these muscles is followed by relaxation and chronic strain. The thinness of the capsule, together with the proximity of bursae, tendons and bones, results in any infection which is primary in one structure soon spreading and involving others. Most persons are subject to constant irritation of their subcoracoid bursae as a result of posture. Limitation of external rotation is more characteristic of subcoracoid bursitis than of any other lesion of the shoulder. It is difficult to rule out a diagnosis of arthritis merely from negative roentgen-ray examination. Extra-shoulder lesions are a common cause of painful, and at times stiff, shoulders. Relaxed capsule is a frequent cause of stiff and painful shoulders. Physical therapeutic measures to counteract atrophy should be instituted at an early period in all cases. Inflammation of many of the structures surrounding the shoulder joint occurs in almost all painful shoulders, and a diagnosis of *periarthrititis* is legitimate when the primary etiologic agent is obscured.

64. Rogers, William A.: *J. Bone & Joint Surg.* 10:104 (Jan.) 1928.

65. King, Jennings M., Jr., and Holmes, George W.: *Diagnosis and Treatment of Four Hundred and Fifty Painful Shoulders*, *J. A. M. A.* 89:1956 (Dec. 3) 1927.

spoken of as "calcium coagulation" formation of bone might readily be established. Examples of such biologic colloid mutations are found in the development of the teeth, of the exoskeletons of animals, and probably in the formation of gallstones and other concretions. The property of reversibility which is peculiar to colloids would amply explain the destructive processes of bone absorption and osteolysis. This conception would therefore give the place of first importance to the collagenous intercellular matrix and regard it as a tissue that retains its vitality and holds in a reversible colloidal state the inorganic salts of bone. Any influence, whether chemical, bacterial, vascular, nervous or glandular, would exert its effect on this substance, which in turn would be reflected in a corresponding alteration in the calcified content.

After referring to the work of R. Robison, who has shown that an ester plays an all important part in the conveyance by the blood of calcium with which it forms soluble salts, Fairbank<sup>61</sup> called attention to the field which this discovery opens. For normal development of bone three things appear to be necessary: (1) a proper cartilaginous or membranous scaffold for the bone; (2) the deposit of the necessary inorganic salts; (3) a sufficient number of normal bone forming cells. The author suggests the following classification of general diseases of the bone: I. Congenital developmental errors; osteogenesis imperfecta; diaphyseal aclasis; dyschondroplasia; achondroplasia; craneocleido dysostosis; myositis ossificans idiopathica. II. Errors of metabolism; scurvy; rickets; renal dwarfism; dwarfism associated with (1) celiac disease; (2) pancreatic disorder; (3) hypertrophic cirrhosis of the liver. III. Endocrine errors; gigantism; acromegaly; mollities ossium; osteomalacia; dwarfism and infantilism of various types. IV. Conditions of unknown origin; fibrocystic disease; leontiasis; osteitis deformans; arachnodactyly. V. Multiple neoplasms.

*Graphic Records of Normal and Pathologic Gaits.*—Schwartz and Vaeth,<sup>62</sup> feeling that a more accurate knowledge of normal and pathologic gaits is essential for the better treatment of persons with deforming limps, invented a mechanical device called a "basograph," with which they can make records of limps for study and comparison with the records of supposedly normal persons. The information obtained thus far by means of these records seems to indicate the value of the machine.

*Limps Caused by Diseases of the Hip.*—Fairbank<sup>61</sup> classified his limps as follows: (1) The short leg limp; (2) the painful limp; (3) the stiff limp; (4) the weak leg limp; (5) the hysterical or functional limp.

dorsal vertebrae, making two loops of fascia between the scapula and the spinal column. An excellent result was obtained in the one patient treated.

*Treatment of Coxa Vara.*—The treatment of persons with coxa vara was discussed by Riedel, Rost and Koenig,<sup>69</sup> each of whom expressed different points of view. Riedel described the operation which he employs. The hip is exposed through a lateral excision, with reflection of the greater trochanter. Then a wedge of bone is removed from the junction of the neck and femoral shaft, care being taken to preserve as many of the vessels as possible and to leave the capsule intact. The fragments are approximated and fixed with Schanz's screws. The trochanter is reattached at a more distal point than originally. Rost, on the other hand, stated that he has obtained excellent results by simple tenotomy of the adductor muscles. The results in patients examined from four to five years after the operation were almost ideal. The gait was nearly normal, and the patients did not complain of subjective disturbances in walking or running. Koenig thought that such an elaborate procedure as described by Riedel was unnecessary; that it was possible to dispense entirely with the use of internal fixative materials, and that Nature always took good care to straighten the fragments after subtrochanteric osteotomy of the femur.

[ED. NOTE.—Coxa vara may be due to so many conditions that we are unable to evaluate these statements without more precise knowledge of the type of coxa vara being discussed.]

*Habitual Dislocation of the Patella.*—In spite of the numerous operative methods for overcoming habitual dislocation of the patella that have been described, Hoffmeister<sup>70</sup> was unable to find any that gave active muscular power to the patella. Feeling the need of this in certain cases, he devised a method of transplanting the tendon of the gracilis muscle into the inner border of the patella. The method has been tried at Lexer's clinic in a number of patients with good results. The gracilis is exposed through a longitudinal incision on the inner side of the knee, cut as far distally as possible, and freed for a distance of from 8 to 10 cm. The free end of the tendon is then pulled beneath the sartorius muscle and fixed under considerable tension in a hole which is drilled in the medial border of the patella. Hoffmeister stated that it does not much matter whether the gracilis, the semitendinosus or the semimembranous is selected for transplantation.

*Fusion of Paralytic Knees.*—Miller<sup>71</sup> performed fusion operations on the knees of twenty-five patients with infantile paralysis, in whom

69. Riedel, Rost and Koenig: *Zentralbl. f. Chir.* 55:948, 1928.

70. Hoffmeister, W.: *Zentralbl. f. Chir.* 55:65, 1928.

71. Miller, O. L.: *South. M. J.* 20:782 (Oct.) 1927.

*Treatment of Tennis Elbow.*—Mills<sup>66</sup> pointed out that many patients with tennis elbow have been relieved by osteopaths, bone setters, etc. The author observed in this condition that full pronation with complete wrist and finger flexion caused limitation of extension of the elbow. By manipulating the elbow into complete extension with the hand and forearm in this position, while at the same time pressing over the external epicondyle, the author was able to relieve the symptoms in all patients so treated. In patients with symptoms of long standing, the author advocated the same manipulation, only with the aid of an anesthetic. He regarded the condition as due to the impingement of a torn part of the orbicular ligament between the radial head and the capitellum, thus simulating displaced semilunar cartilage of the knee joint.

[ED. NOTE.—We do not agree with the author's interpretation of the pathologic condition of tennis elbow, and we are inclined to believe him overenthusiastic as to the results of manipulative treatment. If manipulation proves of value, the explanation is likely to be found in the stretching of inflamed and contracted tissues in the region of the epicondyle.]

#### OPERATIONS ON THE BONES, JOINTS AND TENDONS

*Repair of Nerves and Tendons of the Hand.*—Bunnell<sup>67</sup> reported an unusually interesting series of cases of repair of nerves and tendons in the hand. Thanks to a meticulous technic and painstaking study of the disabilities, he was able to secure a high percentage of successful results. His technic is rigidly aseptic and atraumatic. The work is done under ischemia to furnish perfect vision and to avoid the trauma of sponging. "After winding the limb with an Esmarch bandage from the fingers to the elbow, a blood pressure band is placed on the upper arm and pumped to 250 millimeters of mercury. All of the dissecting and fine work is completed before the tourniquet is released, and this should not be longer than one hour, or some degree of induration and reaction will result. On releasing the tourniquet firm pressure is made with sponges on the wound until hemorrhage from the smaller vessels has stopped. Triple O catgut controls the rest." For joining tendons, Turner's patent ligature silk is used. Bunnell reported success with long free grafts of nerves and tendons.

*An Operation for Slinging a Drooped Shoulder.*—Henry<sup>68</sup> described an operation which he has performed for the relief of paralysis of the trapezius muscle with dropping of the shoulder. The scapular border was exposed and two holes drilled in it. From these holes flexible wires were passed around the spinous process of the sixth cervical vertebra.

66. Mills, Percival: Brit. M. J. 1:12 (Jan. 7) 1925.

67. Bunnell, Sterling: J. Bone & Joint Surg. 10:1 (Jan. 1928).

68. Henry, Arnold K.: Brit. J. Surg. 15:55 (July 1927).

by flexing the knee. The sharp pointed bodkin was then passed through the posterior ligament of the knee from behind forward and made to follow the course of the posterior crucial ligament. 5. A small incision was now made over the subcutaneous portion of the internal condyle of the femur and a hole drilled through to the intercondylar notch. The end of the tendon was threaded on a flexible wire probe and pulled out through this opening. 6. The knee joint was next placed in full extension, the tendon drawn taut, and its terminal end sewn down to the internal lateral ligament. The incisions were closed and the knee immobilized in a plaster casing. Plaster fixation was discontinued at the end of two months. The authors reported that at the end of three years the patient walked with a normal gait, had a full range of motion and had worked as an ordinary laborer. His only complaint is that the joint is a little weak, and this is explained by the fact that there is still a little excess of lateral and anteroposterior mobility.

[ED. NOTE.—The operation described appears to offer an ingenious answer to the perplexing question of how to repair a torn posterior crucial ligament. It satisfies the anatomic requirements better than any other procedure of which we have heard.]

*Osteotomy of Malleolus.*—Pieri<sup>74</sup> suggested a wedge shaped osteotomy of the external malleolus as a means of overcoming the residual varus deformity of the ankle after an old varus deformity of the foot has been corrected as thoroughly as possible. He employed the following technic: A cuneiform osteotomy of the external malleolus is performed, and a wedge of bone with its base external and with a width of approximately 1.5 cm. is removed. A transverse osteotomy of the internal malleolus is next performed from the inner side, the varus deformity of the ankle corrected, which closes the opening in the external malleolus and makes a wedge shaped gap in the internal malleolus into which he fits the wedge removed from the external malleolus. He reported satisfactory results in two patients and the roentgenograms were printed and showed good anatomic correction.

*Operative Correction of Drop Foot.*—Lambrinudi<sup>75</sup> noted that an operation to fix the os calcis to the astragalus with the latter in a position of permanent equinus, but with the foot at right angle alinement with the leg would be an effective means of checking foot drop. By a lateral J-shaped incision exposing the astragalus, os calcis and scaphoid, he removed the cartilage from the subastragalar joint. He then resected the lower portion of the scaphoid and the head and part of the neck of the astragalus in such a way that when the astragalus is tilted the forward edge may be locked under the scaphoid. The portion removed

74. Pieri, Gino: *Chir. d. org. di movimento* 6:616 (Nov.) 1927.

75. Lambrinudi, G.: *Brit. J. Surg.* 15:193 (Oct.) 1927.

it appeared improbable that there would ever be sufficient muscle recovery to enable the patient to go without a permanent brace or crutches or without using the hand to reinforce the quadriceps muscle. The age of the patients ranged from 9 to 16 years. The operation consisted in shearing off the articular cartilage from the femur, tibia and patella. The patella was used as a graft across the gap between the femur and tibia. The epiphyseal cartilages were not damaged. Ankylosis was obtained in all cases.

[ED. NOTE.—We believe, in general, that fusion of the knee in infantile paralysis is to be condemned, but there are special circumstances which occasionally may justify it.]

*Injuries to Semilunar Cartilages.*—Fagge<sup>72</sup> discussed the etiology of torn internal semilunar cartilages, particularly of the bucket-handle type, which is commonest of all, and in his opinion perhaps primary to all other types. His conception of the sequence of events at the time of injury is that the knee is first abducted and the internal meniscus sucked toward the center of the joint; then the free thin edge of the cartilage becomes fixed, due to rotation in the joint, and with the extension which follows, the internal lateral ligament is pulled tense and the thick edge of the cartilage drawn away from the fixed internal edge, thus causing a splitting of the cartilage.

*Operative Repair of Posterior Crucial Ligament.*—Galle and LeMesurier<sup>73</sup> described an operation for the repair of a torn posterior crucial ligament of the knee. The steps of the operation were as follows: 1. Through a long medial incision at the posterior aspect of the knee, the tendon of the semitendinosus was exposed and freed. It was detached from the muscle as high as possible in the thigh. By way of the superficial portion of the split patellar incision, the fixation of the semitendinosus on the inner surface of the tibia was exposed and the detached portion of the tendon drawn through the front of the leg. 3. The lower portion of the posterior medial incision was then deepened and the space between the gastrocnemius muscle and the tibia widened until the posterior ligament of the knee joint and the lower portion of the posterior surface of the tibia came into view. A hole in the tibia was then drilled from behind forward, the front of the joint emerging near the insertion of the semitendinosus. The cut end of the tendon was then fastened into the butt end of a strong post, the post and passed through the drill hole to the back of the knee. The knee joint was next opened by a split patellar incision and the crucial ligament

72 Fagge, C. H.: Brit. J. Surg. 15:273 (Oct.) 1927.

73 Galle, William F., and LeMesurier, A. B.: Brit. J. Surg. 15:277 (Oct.) 1927.

the opinion that prolonged immobilization retards normal healing and function.

*Disability and Cost of Industrial Fractures.*—Gray,<sup>78</sup> the medical referee for California of the Aetna Life Insurance Company, made a study of the disability and cost of industrial fractures in respect to whether the patients had been treated by specialists or general surgeons. He summarized as follows:

In conclusion, our tabulation shows that the surgeon who has been specially trained in the treatment of fractures produces far better results in serious fractures, but that the general surgeon does more efficient work with minor fractures. In major fractures the added cost produced by the specially trained surgeon is more than compensated by decreased disability. This is not true in minor fractures.

*Operative Treatment of Fractures.*—Discussing the treatment of persons with fractures by open operation, from the development of which he expects future progress in the treatment of persons with fractures, Scudder<sup>79</sup> stated his belief that under present conditions fractures can be divided into three groups: (1) Those never operated on, such as Colles' fractures, fractures of the clavicle, many fractures in childhood or the adolescent period, and many fractures occurring at birth; (2) those always operated on, such as fractures of the patella with wide separation of the fragments, fractures of the head or neck of the radius, with such displacement of the small proximal fragment that there would result without operation great limitation of pronation and supination, certain spiral and oblique fractures of both bones of the leg in the middle or lower third, fracture of the os calcis, in which the line of fracture enters the astragalocalcaneal joint, fractures of the olecranon with wide separation, fracture of the shaft of the radius with displacement and irreducible fracture of the shaft of the femur; (3) those in which operation must be looked on as of doubtful applicability, such as fractures of the humeral shaft above the middle and near the shoulder joint, of both bones of the forearm and, of course, many others.

*Influence of the Surgical Experience During the Great War on Treatment of Persons with Fractures in Great Britain.*—According to Bristow,<sup>80</sup> the World War taught three great lessons in the handling of fractures: first, the value of Thomas' splint; second, the necessity for the segregation of fractures, and third, the value of team work. The postwar experience has shown that there is great need for

78. Gray, R. N.: *J. Bone & Joint Surg.* 10:27 (Jan.) 1928.

79. Scudder, C. L.: *Indications for Operative Treatments of Fractures*, J. A. M. A. 89:1917 (Dec. 3) 1927.

80. Bristow, W. R.: *Influence of War Surgery on Treatment of Fractures in Great Britain*, J. A. M. A. 89:1920 (Dec. 3) 1927.

from the front of the astragalus is reshaped and placed at its posterior surface to act as a block between that and the os calcis. The operation has been performed nine times, with seven successful results and two failures, the latter due to slipping of the anterior edge of the astragalus from beneath the scaphoid. The author stated that there should be good power in the gastrocnemius for this procedure to be effective.

*Results of Stabilization of Paralytic Feet.*—Campbell<sup>76</sup> reported the results in 213 patients in whom he employed his bone block operations. Of the patients, 104 were children and 109 adults. Of the 104 children, seventy-six met all requirements in determining the end-results, while in twenty-eight either sufficient time had not elapsed or the patient was not available for observation. In seventy-one of the seventy-six, excellent results were obtained, the bone block being effective and preventing plantar flexion by impingement of the block either against the posterior aspect of the tibia or the rim of the articular surface of the tibia. There were five failures, three of which were due to improper technic at operation as demonstrated by roentgenograms. The transplants were placed too far posterior to the ankle joint to be effective in preventing plantar flexion. In one a good result was apparent after a few months, but was followed by a gradual dropping of the foot downward, though the size and relation of the bone block were satisfactory. This relapse was apparently caused by increased relaxation of the ligaments of the ankle joint. In one, apparatus was apparently discarded too early, as the unorganized graft and callus permitted plantar flexion from the constant force of gravity. Campbell stated that the bone block method has been of value in practically all persons with paralytic deformities of the feet with the exception of cavus, calcaneus and calcaneovalgus. Stabilization of the foot has been rendered more positive by the bone block and by the additional fusion of the astragalus and calcaneus through the block.

#### FRACTURES

*Review of Two Thousand Fractures.*—Newell<sup>77</sup> published a review of 2,000 fractures in patients personally treated during the past seven years. In this group, there were sixty-four patients who were treated by open operation. The frequency of operation in respect to the different bones was fractures of the radius and ulna first, of the tibia and fibula second, and of the patella third. The fractures included all parts of the body, the lower extremity ranking first. There was only one instance of nonunion and only one of Volkmann's contracture. Open reduction was performed in almost all cases of fracture of the patella and in depressed fractures of the zygomatic arch. The author expressed

76. Campbell, W. C.: *Am. J. Surg.* 3:62 (July) 1927.

77. Newell, E. D.: *South. M. J.* 20:644 (Aug.) 1927.



Free movement of fragments does not inhibit the normal repair process, but if fractured ends of low vitality rub against each other, the bone fragments cannot rub against each other without becoming reduced in vitality and friction facets speedily develop which are similar to the occlusal and interproximate facets on the teeth. Such facets develop within two weeks after the fracture and are usually described as polished or eburnated areas. These are found most often in fractures of the ribs but may occur in long bones. Endosteum or cancellous tissue is of great importance in bone repair. Compact tissue takes little part compared with the endosteum and cambium layer in the formation of new bone. It acts as the scaffolding on which the new bone is laid down. When cancellous tissue is relatively most abundant and mobility feeble or absent, repair is quickest, namely, in vertebrae and in fissured and "greenstick" fractures.

*Fractures About the Elbow.*—Sixty patients with fractures about the elbow were studied by Conwell.<sup>82</sup> Only two of these were treated by open reduction. In the author's opinion, open reduction should be performed only when repeated attempts at manipulative reduction fail. He does not consider the presence of swelling about the elbow a contraindication to immediate closed reduction. He fixes the elbow by a special type of traction apparatus and permits active motion, as soon as the patient is able, to the limit permitted without pain.

Allison<sup>83</sup> laid down the following rules for the treatment of persons with fractures about the elbow:

1. Always give consideration to three factors in fractures of the elbow: (a) injury of the bone; (b) injury of the nerves, and (c) circulatory damage.

2. Haste is unnecessary. Take roentgenograms of the region of injury in two planes. Get a rough estimate of the condition of the peripheral nerves and record it. Form an estimate of the condition of the circulation in the forearm and hand and record it.

3. For the treatment of simple fractures, acute flexion is the rule, but before fixing the elbow, make sure that the fracture is reduced. Watch the circulation of the hand.

4. Difficult fractures of the elbow involving the joint, including those with much comminution or displacement or with accompanying dislocation, require hospitalization and the utmost of surgical skill.

5. In the after treatment, use of the part should be permitted and active exercises encouraged. "Pump handle" manipulation should be avoided.

82. Conwell, H. E.: South. M. J. 20:579 (Aug.) 1927.

83. Allison, Nathaniel: Fractures About Elbow, J. A. M. A. 89:1568 (Nov. 5) 1927.

these lessons to be appreciated today as in war time, both from the point of view of the best care of the patient and from the aspect of teaching.

*Phenomena of the Early Stages of Bone Repair.*—The results of fifteen years' observation of specimens coming to the Western Reserve Anatomical Laboratory and the conclusions derived from them concerning the phenomena of the early stages of bone repair were reported by Todd and Her.<sup>81</sup> According to them, the principles of bone repair are simple and their application varied. The fragments show erosion and vascularity. Part of the erosion is due undoubtedly to removal of the bone vitalized in the actual process of fracture, part to the channelling of old bone adjacent to the fracture by the multiplication of blood vessels which are bringing the necessary pabulum for nourishment of the repair cells. On the eroded areas of the fractured and adjacent surfaces, sub-periosteal and endosteal or caseations, there appears a callus of varying texture, finely granular in unimpacted fragments, lava-like in those which were permitted to heal. By successive stages, this callus is transformed into a cancellous mass and later into tissue with haversian systems. The periosteal and endosteal callus becomes reduced or eliminated and the former is replaced by a cortical bony surface is developed. Definitive callus, of course, remains and goes through the corticization process also. There is no difference in the actual speed of development of these stages in different sites or fractures, but it is natural that a complete fracture cannot be totally bridged as quickly as an incomplete one. Hence, although the same features are to be observed in a complete as in a totally ununited fracture, and although they are to be found at the same date, the so-called or "greenstick" fracture will be completely healed in about twenty days, whereas a complete long-bone fracture may after the lapse of that time show large masses of heaped up lava-like callus with as yet an unbridged gap. An impacted fracture, say of a vertebral body, may be healed in thirteen days. Inequality of vigor in repair is characteristic of the several parts of any fracture. In certain specimens this can be directly referred to bone damage by stress or strain at the actual instant of fracture, but in others the probable cause is more obscure. Where the periosteum is elevated from the bone adjacent to a fracture the bone often is diminished in vitality, does not show erosion and does not take an active part in repair, although it is not dead and becomes ultimately passively incorporated in the new structural bone. It must not be inferred that the raised periosteum develops new bone. As a rule the cambium layer is destroyed, and new bone is formed at or over the stripped surface. Such instances are found more frequently in fractures of the ribs than in the long bones, and they never occur in vertebrae so far as the Western Reserve Anatomical Laboratory collection shows.

81. Todd, T. W., and Her, D. H. *Ann. Surg.* 86:715 (Nov.) 1927.

industrial cases of compression fracture, found that the minimum period of disability before the case was seen by an impartial referee was 17.7 months.

2. When suspicion is aroused it should be confirmed or allayed by accurate roentgenologic films taken in both the anteroposterior and the lateral plane; if doubt remains, stereoscopically as well.

3. Complicating fractures of the laminae, transverse processes or of the ribs and of the bones of the extremities, especially of the os calcis, are often present and influence treatment.

4. In early uncomplicated cases, adequate nonoperative methods may be expected to restore full wage earning capacity.

5. In old cases presenting symptoms, the reduction of the postural faulty mechanics may be expected to relieve the pain and in many cases, the disability as well. If nature has not ankylosed the injured region of the spine, and the patient is to return to back bending labor, ankylosing operations after the faulty mechanics have been corrected are likely to save time and allow the patient to labor without apprehension.

*Fractures of the First Cervical Vertebra.*—Jefferson<sup>87</sup> collected reports of sixty-five cases of fracture of the atlas. He pointed out that in thirty-two cases reported since 1900, only five patients died. The advent of the roentgen ray, making diagnosis possible, has led to an apparent reduction in the number of deaths. The location of these fractures was as follows: anterior arch alone, eight cases; posterior arch alone, twenty-nine cases; both arches, twelve cases; lateral mass, seven cases; transverse process, three cases. A longitudinal compression of the head on the spine was the most common cause of this injury. The complicating injuries were fracture of the odontoid process (seventeen cases), rupture of the vertebral artery, rupture of the great occipital nerve and injury to the spinal cord or medulla.

*Late End-Results in Ununited Fracture of the Neck of the Femur Treated by the Bone Peg or Reconstruction Operation.*—The end-results of the operative treatment in 146 cases showing ununited fracture of the neck of the femur were reviewed by Albee<sup>88</sup> and summarized as follows:

Five patients were seen early and treated by the Whitman abduction spica with excellent results. Thirteen cases had to be eliminated because of incomplete records. In forty-two of the remaining 128 cases the bone peg operation was recommended; in fifty-three, the reconstruction operation. Six of the former refused operation, and nine of the latter, leaving a total of eighty patients (36 bone peg and 44 reconstruction operations).

In ninety per cent of the bone peg operations the results were excellent or good, and in seventy-five per cent of the reconstruction operations. The interval between the time of operation, and that of the last examination varied from a few months to fifteen years. Function is usually good within six months after operation. When we consider that ununited fracture of the neck of the femur

87. Jefferson, Geoffrey: Brit. M. J. 2:153 (July 30) 1927.

88. Albee, F. H.: J. Bone & Joint Surg. 10:124 (Jan.) 1928.



tive of the method of treatment used, a great amount of motion does not result in any case. In the author's experience, the disability due to ankylosis of the subastragalar articulation, provided the foot was in good weight bearing position, was scarcely recognizable. The tarsal joints developed compensatory hypermobility which gave a fair semblance of the lateral motion of the foot, and heavy work could be done without complaint.

*Fracture of Fifth Metatarsal Bone.*—By means of a report of twenty-one cases, Carp<sup>92</sup> illustrated the tendency which he has noted for a fracture of the fifth metatarsal bone to exhibit delay in healing. He ascribed the tendency to a deficient blood supply. Of these patients, twenty were adults and five showed clinical and roentgenologic evidence of delayed union. All the other patients had clinical symptoms over such long periods that the author thought it fair to assume some interference in bone repair in their cases also. By way of treatment, the author suggested immobilization of the foot and leg by a molded plaster splint and, when possible, weight bearing in the splint before the end of one month.

#### DISLOCATIONS

*Pathologic Dislocation of the Hip Joint.*—Putti and Zanoli<sup>93</sup> reviewed the subject of pathologic dislocation of the hip joint resulting from acute infantile arthritis. They discussed the diagnosis and pathologic changes of the condition and reported fifteen cases with end-results. They considered that closed reduction is usually impossible, contrary to the opinion of the French authors. They described the four methods of intervention employed by them as follows:

1. Reconstruction of the epiphysis and neck of the femur by means of a free bone transplant, the head and neck of the fibula being used (one case).
2. Reduction of the greater trochanter into the acetabulum, followed by subtrochanteric osteotomy to reform the femoral neck (three cases).
3. Simple reduction of the epiphyseal stump (five cases).
4. Plastic reconstruction of the femoral neck (method of Whitman, seven cases).

The authors concluded that Whitman's method is the one chiefly to be recommended.

92. Carp, L.: *Ann. Surg.* 86:308 (Aug.) 1927.

93. Putti, V., and Zanoli, R.: *Chir. d. org. di movimento* 6:539 (Nov.) 1927.



infrequent condition in presumably normal brains for the rolandic vein to be either absent or relatively insignificant, instead of being the outstanding vein of the hemisphere. Such conditions merely indicate the great normal variations of the venous system that occur in the brain and that still appear to be of no significance.

In figure 3 (case 3), one sees a relatively enormous vein over the frontal lobe. This vein is continuous with the sylvian vein as the rolandic vein should be, but it is 4 or 5 cm. anterior to a small rolandic vein which emerges from the brain tissue just below the facial center. In case 5 (fig. 5), the rolandic vein passes from the sylvian as it normally should, but sweeps backward in a crescent, and finally, when approaching the falx, bends sharply forward at a right angle and then again mesially at another right angle. Both of these rolandic variations, however, are only a small part of the composite venous and cerebral abnormalities.

In none of the venous deformities is the size of the vessel abnormal (possibly excepting case 3); rather, it is the number, shape and distribution of the vessels that are abnormal. In this respect the venous changes differ from those of the arteriovenous aneurysms in which the size of the vessels is so striking. In addition to the great size, the venous component of arteriovenous aneurysms also shows great abnormalities in shape, number and distribution. One can always be sure that the lesion cannot be arteriovenous if the veins are of normal size. Moreover, in venous anomalies, aneurysms or tumors, one never sees in the veins exposed at operation pulsating red blood, which is characteristic of arteriovenous aneurysms.

In some instances (fig. 3), the deformation of the cerebral convolutions is even more striking than that of the veins. Many of the convolutions are of relatively enormous size and lack the characteristic shape. They appear like masses of brain tissue, improperly formed. In such cases, doubtless both the veins and the brain tissue are wrapped up in the same fundamental maldevelopment. Case 4 (fig. 4) is another example of a vascular abnormality being dependent on the primary embryonic cerebral defect; the sylvian vein received a branch from each side of the cyst and passed along the sylvian fissure as a bifid trunk. In this case the temporal lobe did not have any attachment to the parietal lobe, except in the depth of the brain.

In case 7 (fig. 7) there was a venous plexus in the sylvian fissure of each side and eight or ten additional small plexuses in the pia-arachnoid over both cerebral hemispheres. In this patient there were two other associated cerebral deformations: (1) absence of the corpus callosum, (2) stricture of the aqueduct of Sylvius with resulting hydrocephalus. The child was an imbecile.

Cerebral and vascular deformations are, therefore, commonly associated. The one may cause the other, or, as in case 5, they may be





Perhaps there is more reason for a later origin in arteriovenous lesions, for they have a definite tendency to increase in size. One can conclude only that any cerebral lesion is always a potential source of epilepsy, and that the time element is uncertain for reasons that are not known.

#### REPORT OF CASES OF VENOUS ABNORMALITIES OF THE BRAIN

##### CASE 1.—*Venous Anomaly of the Brain.*

A boy, aged  $3\frac{1}{2}$  years, was referred by Dr. Rosenberger of Milwaukee because of blindness. Two weeks before admission to the Johns Hopkins Hospital, the patient had begun to stumble over objects, apparently because he did not see well.

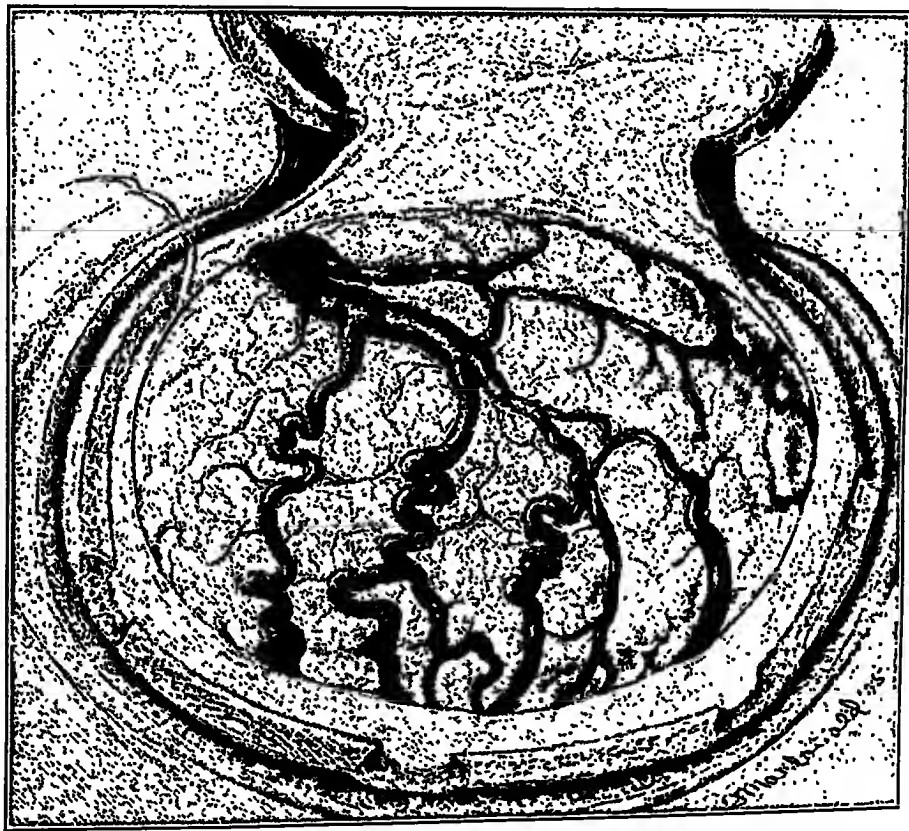


Fig. 1 (case 1).—Field of operation showing the venous anomaly.

He was unable to recognize pictures which he had known perfectly before this time. Since then he had been unable to see at all. There had never been convulsions or any other symptoms. The results of the neurologic examination were entirely negative with the possible exception of the eyegrounds. There seemed to be pallor of the optic disks, though perhaps this was questionable. The x-ray examination of the head was normal.

A suprapituitary tumor was suspected because of the blindness and questionable optic atrophy as suggested by the ophthalmoscopic examination.

The right ventricle was uniformly smaller than the left.

*Operation.*—Right craniotomy was performed to expose the optic chiasm (fig. 1). A series of four tortuous and somewhat enlarged veins converged from the frontal and parietal lobes to the sylvian vein. Except that the sylvian vein

entirely independent and referable to a faulty general development in the embryo. In cases 2, 5 and 6, tremendous vascular deformations were present, in that many vessels of fairly uniform size radiated from the sylvian vein. In such cases the vascular bed becomes a space occupying lesion of considerable size and doubtless acts as a tumor, for in each instance the epileptic seizures were focal and began in the face, i.e., the part of the motor area nearest the tumor. Surrounding this vascular bed, there is always a pool of fluid in the subarachnoid space, and usually the leptomeninges over the affected areas are thickened and often opaque. The brain tissue beneath is also softened and the convolutions atrophied as compared with the surrounding unaffected brain tissue. In case 6 (fig. 6) ventriculograms demonstrated that the vascular bed had indented the body of the lateral ventricle. As seen at operation, the network of vessels was so dense that the underlying brain was entirely obscured.

Another abnormality not infrequently seen is the tortuosity of veins. This is shown in a series of anomalous veins in case 1 (fig. 1). Not infrequently one sees many of the smaller terminal veins tortuous when the larger trunks are not affected. In a recent case of a congenitally deformed brain, a series of eight or ten such venules diverged from the center of the frontal lobe, some going to trunks entering the sylvian, rolandic veins, and others to frontal veins passing to the longitudinal sinus. This tortuosity of some of the smaller veins was also present in case 5 (fig. 5). In this case there was also a diverticulum (venous aneurysm of the superior longitudinal sinus).

#### CLINICAL FEATURES OF VENOUS ABNORMALITIES

With two exceptions (cases 1 and 7) these patients were operated on to find the cause of jacksonian epilepsy. The patient in case 7 was operated on for hydrocephalus; the vascular tumors therefore were incidental. Operation was performed in case 1 because of blindness, and the vascular changes were also incidental. Three of the patients (cases 2, 4 and 7) had varying grades of mental retardation. Another was too young to judge the mental status (case 6).

Two patients (cases 2 and 3) had some slight evidence of motor weakness of the opposite side of the body. In both of these patients the motor weakness was increased for a short time after the epileptic seizures. In one patient (case 5), the epileptic seizures did not begin until he was 28 years old, and in another patient (case 3) the attacks began when he was 13 years of age. The other patients developed convulsions at 5 months, 8 months and 2½ years of age. The time at which convulsions develop from a cerebral lesion is most variable, as these results indicate. The remarkable fact is that a lesion can exist for twenty-eight years without causing trouble and then without apparent reason convulsions will suddenly appear. In arteriovenous aneurysms, the time of onset of attacks may be delayed until much later in life.

these attacks; but later they had been an aura of a convulsion. The seizures came on about every two weeks. After a convulsion, the left side was partially paralyzed for several minutes.

*Operation.*—A right craniotomy was performed on Feb. 19, 1927. The striking observation was the large vein which came out of the posterior part of the frontal lobe about midway between the falx and the sylvian vein (fig. 3). It passed downward into the sylvian vein. A small inconspicuous rolandic vein was about 4 cm. posterior to this anomalous vessel and it had no visible connection with the sylvian vein. The size of the big frontal vein raised the question as to whether an arteriovenous aneurysm might not be beneath, but the blood in the vein was not definitely redder than normal; pulsation could not be seen in the blood stream; nor could a thrill be felt. Even more striking than the venous abnormality was

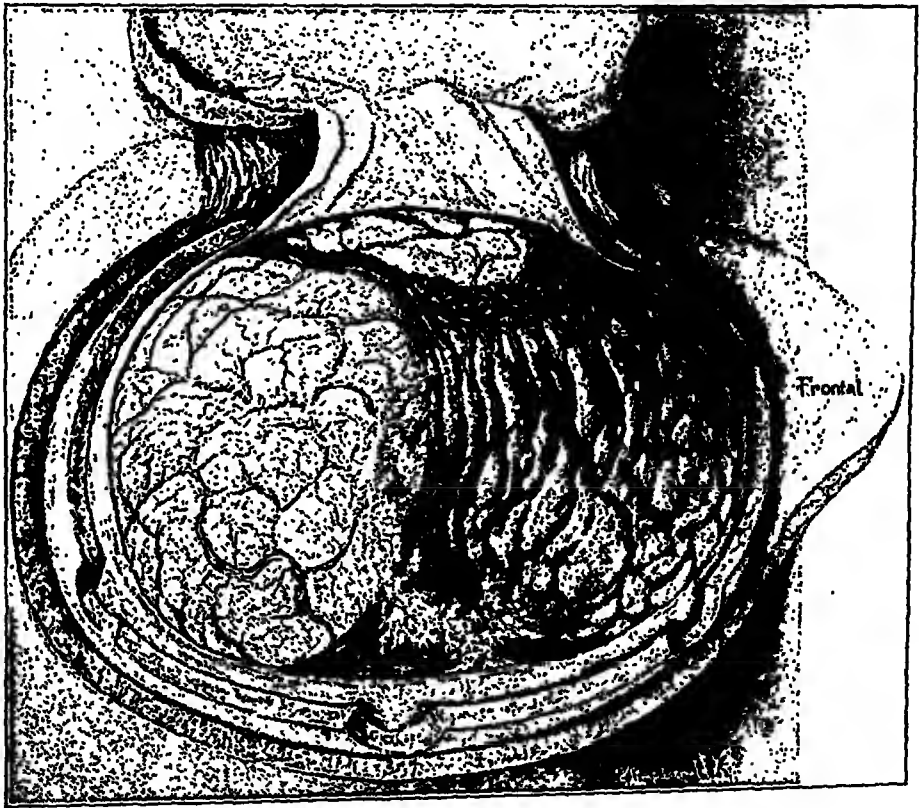


Fig. 2 (case 2).—Venous and cerebral anomalies.

the great deformation of the convolutions in the frontoparietal region. Several were of enormous size and markedly irregular. Nothing could be done to help the patient. The presence of the old hemiplegia still leads one to wonder if a deep vascular lesion may not be present.

*CASE 4.—Venous Anomaly of the Brain.*

A physician's child, aged 3 years, was mentally backward, unable to raise the head and had frequent convulsions. When 8 months old, he had had convulsive twitchings in the left side of the mouth and face. A month later, there had been a series of generalized convulsions lasting several hours. For the next two years he had had two or three convulsions daily, but for six months before operation they were absent. There has been practically no mental development. For several months he had been getting weaker and had taken food poorly.

was larger than usual and bifid for some distance, it was not abnormal. The cisterna chiasmatis was so large that there was a question at the time as to whether this could have caused the blindness. During his stay in the hospital the blindness persisted, but a report two years later stated that his vision was normal again.

Viewed in retrospect, the operative observations did not explain the blindness, nor had the vascular conditions which are here reported caused trouble. They were merely evidences of a congenital maldevelopment in the brain.

*CASE 2.—Venous Anomaly of the Brain.*

A girl, aged  $3\frac{1}{2}$  years, was referred by Dr. Walter Cox of Winchester, Va., because of focal epilepsy. Birth had been normal and easy, and had occurred at full term. When the infant was 5 months of age, it had first been noticed that the normal mental response, evidenced by smiling and holding up the head, had not appeared. When she was 8 months old, definite signs of retardation had been noted. When 1 year of age, the right arm and leg had been less developed than the left, and attempts to hold up the head had been unsuccessful. When 18 months old, she had seemed to see things, but did not fix her attention on objects or persons for any length of time. She has never learned to walk or talk. When  $2\frac{1}{2}$  years of age, she had had the first convulsion, which had lasted about a minute. The eyes rolled up at the onset of the attack, the right hand drew up, then the leg and soon the entire body was involved in a clonic convulsion. She was unconscious about an hour. Numerous convulsions of similar type had since recurred. On one occasion, six or seven attacks had followed in quick succession. Incontinence of urine and even of feces had been noted. There had been many attacks of petit mal type, evidenced by a momentary staring expression.

*Examination.*—The child could not stand or talk. She responded with a silly grin when questions were asked. The right side of the body was relatively underdeveloped, though the arm and leg moved freely. There was also slight facial asymmetry. The deep reflexes were increased on the right side.

A probable diagnosis of a congenital lesion of the left cerebral hemisphere was made.

*Operation.*—Left craniotomy was performed. A large collection of fluid (subarachnoid) covered the anterior half of the exposed area of brain. Over the frontal region, the fluid was at least 1 cm. deep. Through this fluid, and better after its evacuation, five separate interlacing veins (a venous plexus) were seen which filled the sylvian fissure (fig. 2). From this series of veins, twelve or thirteen parallel branches passed across the frontal and parietal lobes to the superior longitudinal sinus. The convolutions of the frontal and parietal lobes were pale, soft, depressed and irregular. The convolutional markings of the temporal lobe were much less affected, but strikingly abnormal also. The subsequent course of the patient was unimproved.

*Anatomic Diagnosis.*—There was an extensive congenital maldevelopment of the brain. In this, the vascular system shared extensively forming a bed of vessels which almost obscured the frontal lobe.

*CASE 3.—Venous Anomaly of the Brain.*

A boy, aged 14, entered the Johns Hopkins Hospital because of convulsions. Since birth the left side of the body had been smaller and weaker than the right. Mentally, he had been somewhat precocious. One year before admission to the hospital, he had had the first convulsion, which had begun in the left side and which had quickly become generalized. For two years previously, he had had spells of tickling sensation in the left side of the face. No attention had been given to

the surface of the brain (adhesions and meningeal thickening). Moreover, if an acute abscess had broken into the ventricle, death undoubtedly would have been the outcome. The failure of the child to develop mentally doubtless denoted other congenital cerebral malformations in the left hemisphere. The child survived the operation, though benefit did not result.

**CASE 5.—*Venous Anomaly of the Brain; Also Venous Aneurysm of the Longitudinal Sinus.***

A large, strong miner, aged 29 years, was referred because of jacksonian convulsions. Eight months before admission to the hospital, when picking berries, he had had a severe headache in the left temple. This had lasted a few days, when he had had the first generalized convulsion. There was an aura of pain in the teeth on the right side. He had had nine other major attacks since then,

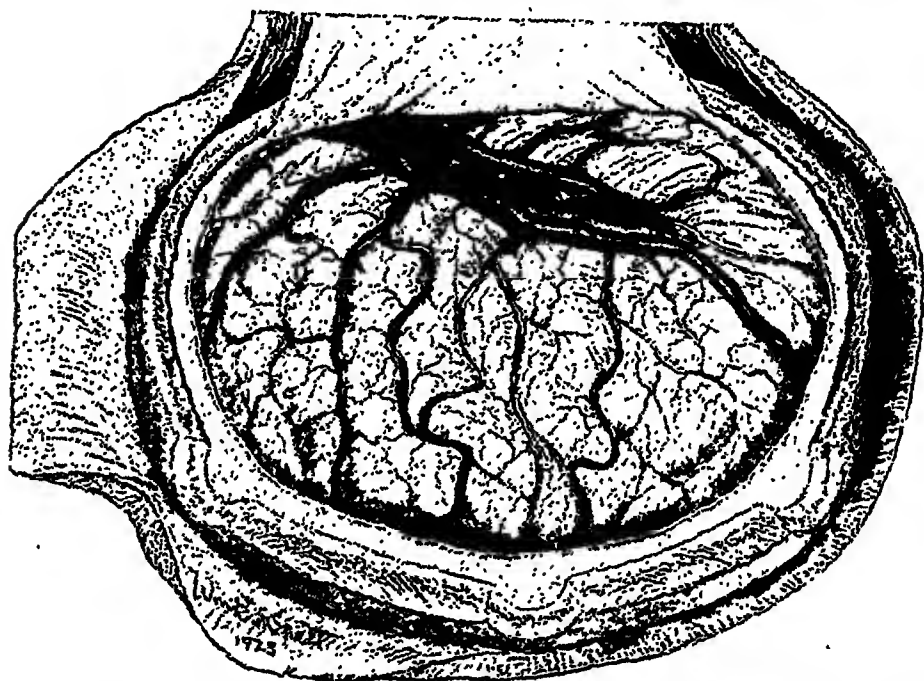


Fig. 4 (case 4).—Venous and cerebral anomalies. A cyst presenting in the sylvian fissure is responsible for bifid sylvian vein.

in all of which his right hand and face first began to contract. Mental change, dizziness or vomiting was not noted.

The results of the physical and neurologic examinations were entirely negative. The Wassermann reaction of blood was negative.

**Operation.**—A left craniotomy was performed on March 14, 1928. Aside from two little arachnoid villi which had perforated the dura and formed small knoblike papillomas between the dura and bone (the cause of their formation and their significance, if any, is not clear), nothing abnormal was encountered until the brain was exposed. A striking, congenitally malformed brain was disclosed. The arachnoid was thickened and the subarachnoid fluid formed a large pool over much of the exposed brain. This bed of fluid was particularly deep over a greatly widened sylvian fissure into which nineteen veins of varying size converged from the frontotemporal and parietal lobes. They passed into the sylvian and rolandic veins. The rolandic vein was very large and abnormally placed. It made a big bend posteriorly after leaving the sylvian vein and when about 3 cm. from the

When 3 months of age, the patient had had a high fever and a rigid and retracted neck; examination of the spinal fluid revealed 76 cells. Shortly after this attack, his right eye had become crossed, and he had lost the use of his left arm and leg. He had become emaciated and had been unable to move the head for some time. Gradual improvement had followed during the next few months, and the function of the left leg had returned entirely, but the arm had remained spastic and was not used much. It was five months after this illness when the first convulsion developed, beginning in the left side of the face (the affected side).

Physical and neurologic examinations revealed only the slightly spastic left arm which the patient used much less than the right.

The history suggested an old inflammatory lesion, perhaps an old healed abscess.

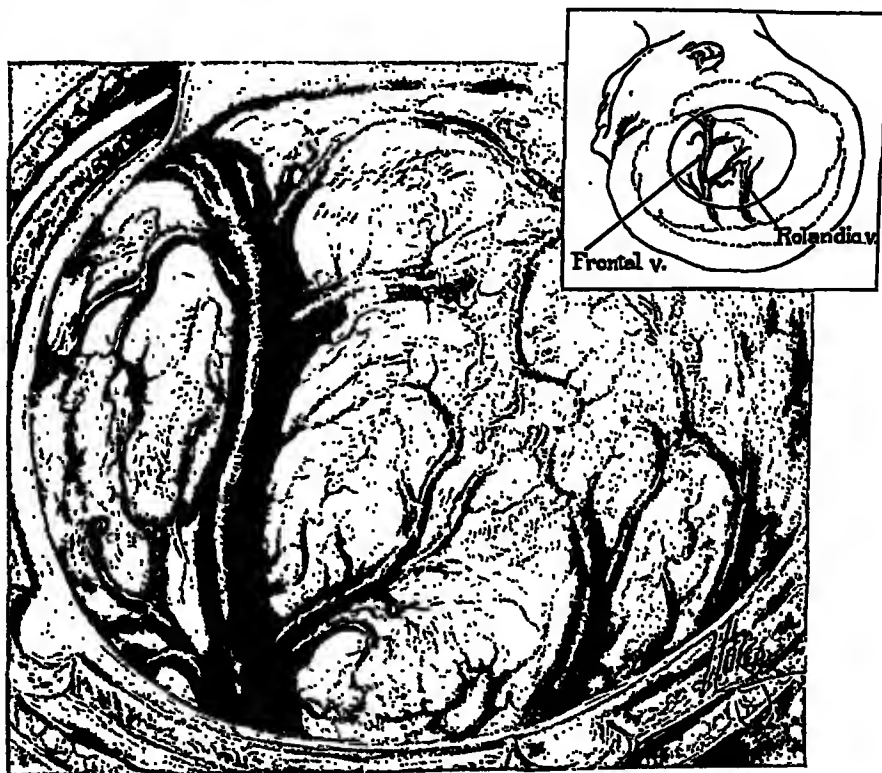


Fig. 3 (case 3).—Venous and cerebral anomalies.

Ventriculography showed a large cavity in the region of the right temporal lobe, filled with air and communicating with the lateral ventricle.

*Operation.*—The right cerebral hemisphere was explored. A large cyst was found between the temporal and parietal lobes (fig. 4), and opened into the body of the lateral ventricle. A branch of the sylvian vein passed on each side of the cyst. The whole temporal lobe as far back as the occipital lobe did not have any superficial attachment to the rest of the branch. The bifurcated sylvian vein surely represented a congenital malformation. The separation of the temporal lobe from the rest of the brain was surely due to a congenital defect and doubtless the big cyst with its communication with the lateral ventricle was another malformation. There were no signs of an old inflammatory process on

The results of the physical and neurologic examinations were negative; also the Wassermann reaction of blood. The family history was negative.

*Operation.*—A small left-sided craniotomy was performed. The sylvian fissure was wide and a roughly circular area extended mesially from it. This area was covered with fluid, beneath which a mass of veins could be seen (fig. 6). After the fluid was evacuated, this cluster of vessels, not unlike a pampiniform plexus of tortuous entwined veins, was more distinct. The vessels completely obscured the underlying brain. They covered Broca's convolution. A second smaller plexus was situated on the temporal lobe about 2 cm. from the large plexus. Several veins bridged the intervening gap and connected the two vascular beds. The vessels were all veins. Palpation did not reveal a thrill nor was pulsation visible. The shape and size of the convolutions were irregular and markedly abnormal.

The operative observations indicated a congenitally malformed brain with venous anomalies.



Fig. 6 (case 6).—Two congenital plexuses of veins in the sylvian fissure. This mass of veins produced an indentation in the body of the lateral ventricle (ventriculogram).

#### CASE 7.—*Veinous Anomalies of the Brain: Veinous Plexuses.*

An infant, aged  $2\frac{1}{2}$  years, was referred by Dr. J. B. Sidbury of Wilmington, N. C., with the diagnosis of hydrocephalus. The head was large at birth; ptosis of left upper lid also dated from birth. At the age of 3 months, the head had grown rapidly, then measuring  $18\frac{1}{2}$  inches (47 cm.). Jerky movements of the extremities had been frequent during the first three months, but there had not been any convulsions. The child had held up her head when she was 6 months of age, and had laughed a month later. She could not sit up alone, though she used her hands and legs in playing. The head did not grow so rapidly after the first six months. At one year of age, it measured  $21\frac{1}{2}$  inches (54.6 cm.); at present ( $2\frac{1}{2}$  years of age) it is only  $22\frac{1}{2}$  inches (56.8 cm.). When the child was  $5\frac{1}{2}$  months of age, the first tooth had appeared; at 1 year there had been twelve teeth. Her condition had remained more or less stationary for the past eighteen months. She could not sit or stand alone, could not feed herself, and could not



longitudinal sinus suddenly turned forward at right angles, and after a course of 4 or 5 cm. again turned abruptly at right angles to enter the longitudinal sinus. No thrill could be felt in the enlarged rolandic vein, nor was there evidence of red arterial blood in the vessel. Over the frontal lobe another series of veins (about eight in all) converged to three larger trunks which entered the longitudinal sinus anterior to the point of entry of the rolandic vein.

After the subarachnoid fluid had been evacuated, the convolutions were seen to be badly misshapen and malformed. Many were large and pointed instead of having the normal well rounded surface. In addition to these abnormalities, a venous diverticulum from the longitudinal sinus was found with the characteristic anatomic conditions described under the cases of this type. This was removed

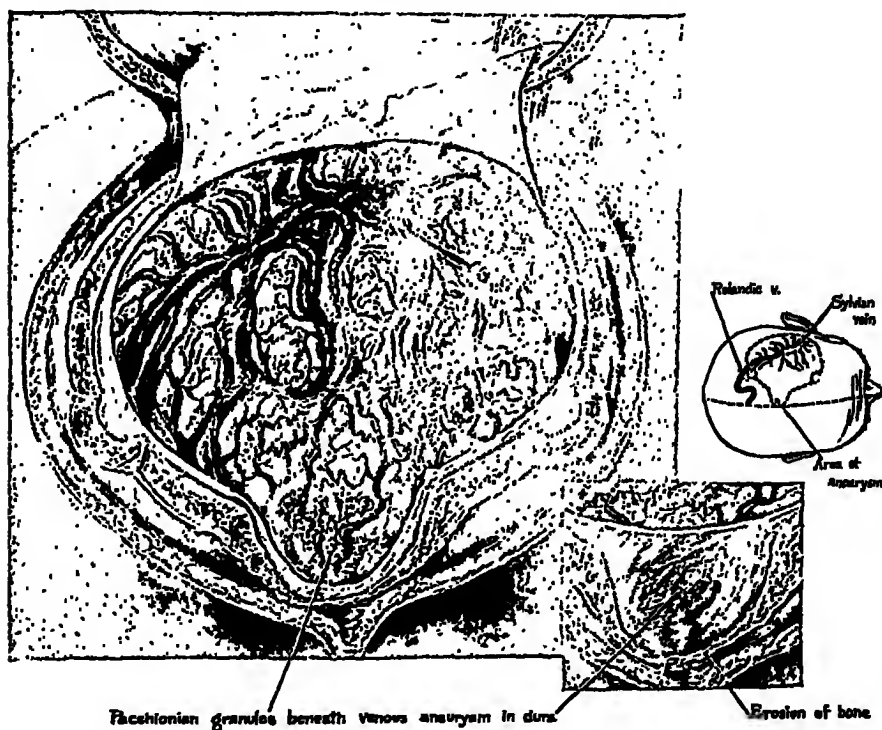


Fig. 5 (case 5).—Drawing at operation, showing masses of veins emptying into the sylvian vein, the abnormal course of the rolandic vein and the venous aneurysm from the longitudinal sinus.

and a fascial transplant sutured in the dural defect. It was not thought that this aneurysm was causing the attacks because they began in the face, but rather that they were caused by the congenital vascular and convolucional ensemble contiguous to the facial center (fig. 5). Nothing could be done to help this.

The postoperative course was uneventful.

#### CASE 6.—*Venous Anomaly of the Brain.*

An infant, aged 5 months, was referred by Dr. J. W. Ames, of Denver, because of jacksonian convulsions beginning in the right side of the face but quickly becoming general. The first attacks had begun a month before admission to the hospital. They had steadily increased in number and severity, and many attacks occurred daily.



who had bilateral symmetrical elevation of the skull, to either side of the longitudinal sinus and slightly anterior to the rolandic area. Although superficially the bony prominence suggested an osteoma, the x-ray examination showed this diagnosis to be incorrect, for the bone was

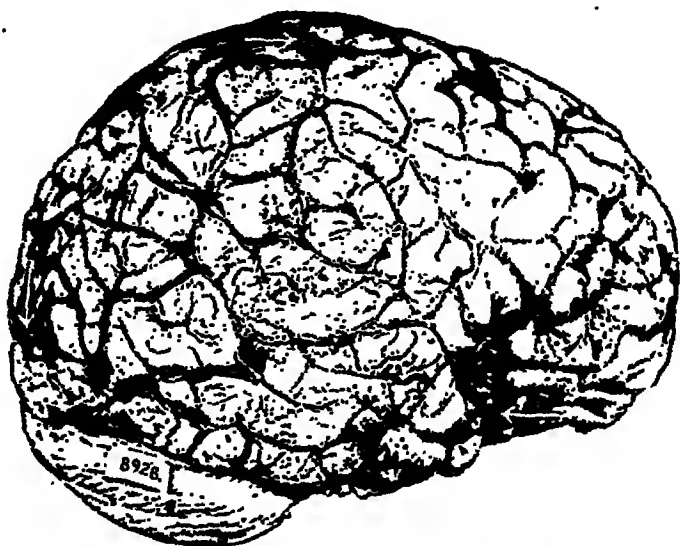


Fig. 8 (case 7).—The venous plexus in the sylvian fissure of the right side of the brain and several small plexiform angiomas over the cortex. The drawing in figure 7 is from the base of the brain.

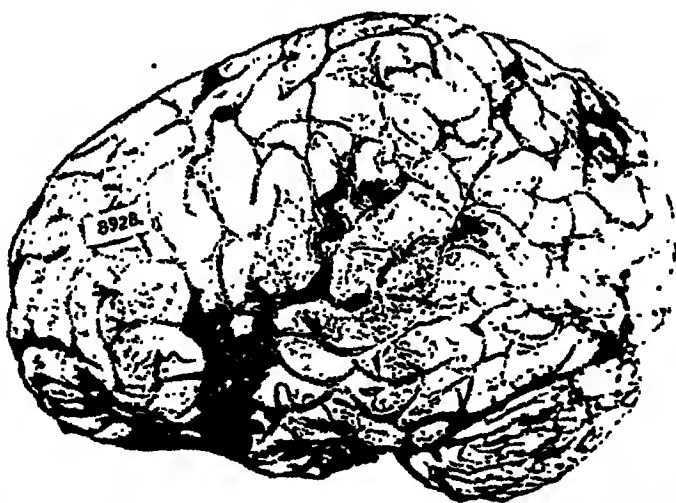


Fig. 9 (case 7).—Left side of the brain showing plexiform angioma in the left sylvian fissure.

greatly thinned in addition to being pushed definitely outward. On exploration of this part of the skull, the sudden thinning of the bone was found to be striking and the dura immediately beneath to be exceedingly bloody, owing to the presence of a well localized dural vascular bed (fig. 10). On turning back the dura, this same localized area was

talk. She gritted her teeth a great deal, particularly when she lost her temper. The fontanels were entirely closed. An obstruction in the ventricular system was shown by the fact that phenolsulphophthalein injected into the spinal canal did not appear in the ventricular fluid.

*Operation.*—The floor of the third ventricle was removed for hydrocephalus. The fissure of Sylvius contained a venous plexus (angioma). The angioma was made up of cerebral tortuous veins which were entwined. Tributaries converged to the venous plexus from the frontal and parietal lobes.

The child died forty-eight hours after operation. Autopsy showed another venous plexus on the other side of the brain and in precisely the same position, which was almost an exact duplicate of the one found at operation. In addition,

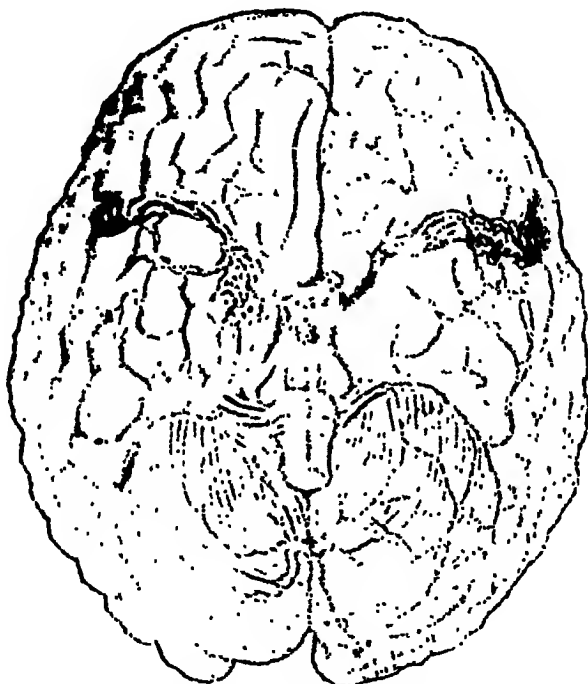


Fig. 7 (case 7).—Congenital plexiform angioma in each sylvian fissure.

there were eight or ten little venous collections of much the same character in the pia-arachnoid membranes over both hemispheres. Each little vascular mass of veins measured from 1 to 2 cm. in diameter, and was flattened on the brain and not elongated like those in the sylvian fissure. They were free in the meninges and could be dissected from the brain. In addition to these vascular abnormalities, the corpus callosum was absent and the aqueduct of sylvius obliterated (figs. 7, 8 and 9).

#### VENOUS ABNORMALITIES IN THE DURA: VENOUS ANEURYSMS?

In a group of four venous aneurysms with focal epilepsy in which the attacks began in the leg or arm, an anatomic observation was so uniform and so striking that I venture to suggest an etiologic relationship. The lesion is a diverticulum of the superior longitudinal sinus—a venous aneurysm. My attention was first drawn to this condition in a patient

size, remains on the opposite side and has not caused any symptoms. If the x-ray change is in association with focal convulsions that begin in the leg or arm, and if another lesion in the prerolandic cortex is absent, the existence of the lesion and its causal relationship would seem to be definite.

Brief mention is made of a case in which there was an enormous occipital sinus (case 11, fig. 13). Whether it has any clinical significance is doubtful, but it is an example of a venous anomaly, which may offer great surgical difficulties and dangers if not recognized before it is opened. This sinus, while normally present, may be and not infrequently is entirely absent, and when present its size is most variable, though rarely over 1 cm. wide. In one patient, a hydrocephalic infant, the occipital sinus was proportionately larger than in this patient; it was not the cause of the hydrocephalus but was merely another manifestation of a congenital anomaly. In both of these cases, the occipital sinus bifurcated near the foramen magnum and each branch passed laterally in the dura to enter the internal jugular vein at the jugular foramen.

#### REPORT OF CASES OF VENOUS ABNORMALITIES IN THE DURA

##### CASE 8.—*Venous Aneurysm from a Longitudinal Sinus.*

A large, strong man, aged 24, was referred by Dr. W. L. Brown, of El Paso, Texas, in May, 1921, because of recurring jacksonian convulsions. The family and past histories were negative, except for one incident which will be included in the story of his present illness.

The first attack had occurred suddenly six years before admission to the hospital, when the patient was 18 years old. Since that time, they had averaged about two a month, with a tendency gradually to become more severe and more frequent. Every attack came at night just as he was dozing off to sleep. A queer feeling "like a chill" awoke him. In a few seconds the right arm and face began to jerk and then became numb. He then lost the power of speech but was still conscious. He passed into coma as the convulsions became clonic and bilateral. Following the convulsion, he had a queer sulphur taste in his mouth (uncinate attack?). An interesting fact in his history was that when 11 years of age he complained of attacks of numbness of the right arm over a period of nearly a year. This disappeared until the advent of convulsions seven years later.

The results of the physical and neurologic examinations were negative, except for a bony prominence situated in the midsagittal line and extending on each side of the midline; the left side was distinctly a little larger. In the midsagittal plane it was a trifle less than midway between the nasion and the inion. The bony prominence measured about 7 cm. from side to side (bilateral) and 3½ cm. anteroposteriorly. The roentgenograms showed a marked localized bulge of the skull in this region with great thinning of the bone from within.

*Operation.*—On May 28, 1921, left craniotomy was performed, approaching the midline. The brain appeared normal except for the region of the arm and leg centers where the brain was firmly attached to the dura by a mass of pachionian granulations. In front of this restricted area which corresponded exactly with the eroded bone in the roentgenogram, the pachionian granulations and attach-

found to be densely attached to the brain tissue by psammomatous granulations which were absent both in front of and behind the affected area. Moreover, after the fibrous attachments had been separated the underlying brain tissue was distinctly soft (fig. 11). The palpating finger sank into this part of the brain to a greater depth than elsewhere. There was, therefore, a localized softening of the brain immediately beneath a localized vascular bed in the dura, and a localized erosion of the inner table and bulging of the outer table of the skull directly over the same lesion. It was not difficult to believe that any lesion which could produce such striking changes in the bone could also damage the brain and thereby cause epilepsy. Moreover, its location directly in the pre-rolandic leg and arm centers suggests the correlation of the pathologic and clinical data.

In excising this vascular dural mass, which bled freely because the dura was thinned and attached to the bone, it could be seen that it was fed by several channels from the longitudinal sinus, and that it did not have a single wide communication with the sinus. There was no arterial communication with the middle meningeal artery, although the bleeding was so severe as to make one wonder if it might not be an arteriovenous aneurysm. It is also worthy of note that the rolandic vein does not enter into this vascular bed in the dura; it passes into the longitudinal sinus, immediately posterior to it.

This patient had only two attacks during the year following the operation and none in the next six years. The capricious results following any form of treatment in cases of epilepsy make any claims hazardous. Moreover, even though the venous aneurysm is removed, the cerebral defect remains and is in itself always a potential source of convulsions. It is, of course, always advisable to remove the primary cause even if the secondary cerebral defect cannot be altered. The attacks will improve even if the patient cannot be cured.

In the two other cases (9 and 10) which I have classified under this group, the clinical and pathologic observations were such exact duplicates of those in the case just described that additional comment is not necessary. Since the operation in these cases has been performed only during the three months prior to the time this paper was written, too little time has elapsed to consider the results. All patients have made uneventful recoveries after removal of the lesion.

There is perhaps reason to deny the existence of this lesion. X-ray examinations of the skull frequently show in this location a degree of rarefaction which must be looked on as a normal observation—usually it is called a venous lake. But in the cases here described, the normal x-ray changes are exaggerated. Where the normal changes end and the pathologic begin must vary in different persons. In fact, in the case just described (case 8), a seemingly identical lesion, and of the same

A probable diagnosis of venous aneurysms from the longitudinal sinus was made.

*Operation.*—On Jan. 24, 1928, a left craniotomy was performed as in the preceding case (figs. 10 and 11). The bone was very thin over a restricted area about as large as a half dollar. The same venous lakes bled freely and had to be controlled by pressure of the finger. The dura was pulled mesially. The same dense area of pachionian granulations was separated from dense opaque leptomeninges. The same softened zone of brain was immediately beneath. Elsewhere pachionian granulations could not be seen. A fascial transplant was used to replace the dura which was excised and carefully sutured close to the longitudinal sinus.

The postoperative course was uneventful.

*CASE 10.—Venous Aneurysm from the Longitudinal Sinus.*

A well nourished boy, apparently normal mentally and physically, except for convulsions which began in the right leg, gave a past history which was negative



Fig. 10.—The venous bed connected with the longitudinal sinus. This vascular mass caused both erosion of the skull and indentation of and consequent injury to the brain.

except that glands of the neck had been removed eight years before the present examination. There was no history of epilepsy on either side of the family.

The convulsions began three years before admission to the hospital, when he was 11 years of age. There was no antecedent history of trauma or illness which seemed to have any bearing on the onset of the attacks. From the beginning the seizures were of jacksonian character always beginning in the right leg, and almost simultaneously, but a trifle later, in the right arm. Frequently, a numbness of the right leg and at times of the right arm was an aura. A residual weakness of the right leg and less of the arm followed the attack and persisted for several minutes. The convulsions lasted from one to two minutes, were clonic and became general as consciousness was lost. He had never bitten the tongue or lost sphincter control. There was usually sufficient warning to allow him to sit down before

ments to the dura were absent. The lesion was strikingly localized. The bone was then rongeured away over the affected area. The skull became progressively thinner as the longitudinal sinus was approached, where it was about 3 mm. thick. The denuded dura bled furiously from several perforations of the dura which was closely attached to the area of eroded bone. These venous channels were not continuous with the veins which cross from the cerebral hemisphere and are en route to the longitudinal sinus. Rather they were off-shoots from the longitudinal sinus, and seemed to communicate with a common vascular bed, for it was necessary to ligate all the channels as they entered the longitudinal sinus before the bleeding in the dural vascular bed could be controlled. The Rolandic vein passed just posterior to the venous aneurysm to enter the longitudinal sinus. It was not injured. The other interesting feature of the lesion was the firm and dense attachment of the aneurysm to the brain by pachionian granulations. These had to be severed with a knife or scissors. Contiguous to this local area both anteriorly and posteriorly, these attachments were entirely absent. The leptomeninges were greatly thickened and opaque for some distance beyond the aneurysm and the brain was distinctly softer than the surrounding normal brain. Such observations make it difficult to believe that pachionian granulations are other than protective formations against the pressure of large venous channels. In the later years of life, the pachionian granulations develop normally along the rim of brain which lies along the wall of the longitudinal sinus. Doubtless the explanation of these granulations is similarly a reaction to the trauma incident to the flow of blood through the longitudinal sinus.

The entire area of dura containing the venous diverticulum was removed and replaced by a transplant of fascia lata. The dura was divided close to the longitudinal sinus by placing a series of clamps at the base and closing the dural margin with a series of transfixion sutures of silk.

As the convulsions had never primarily attacked the left side of the body, no attempt was made to remove the right-sided lesion, which was a duplicate of that removed from the left.

The immediate postoperative recovery was uneventful. During the first year following operation, the patient had two attacks and has had none in the following six years.

#### CASE 9.—*Venous Aneurysm from Longitudinal Sinus.*

A highly nervous woman, aged 27, was referred because of frequent jacksonian convulsions. The family and past histories were entirely negative. One year before admission to the hospital, she had suddenly felt dazed for a few seconds (*petit mal*). Several days later, she had experienced the same sensation. Two or three weeks later, numbness and stiffness had appeared in her right arm and leg in association with the dazed spells. For several seconds after an attack she could not speak or write, and there would be a transient weakness and numbness of the hand and leg. She had not lost consciousness in attacks at this time. In some attacks, the right side of the face twitched. The numb feeling was associated with the sensation of an electric shock passing through the right side of the body. There had not been generalized convulsions. On one day, a few weeks prior to operation, the attacks had come every ten or fifteen minutes. A day seldom passed without the occurrence of severe attacks. Headaches were never present.

The results of the physical and neurologic examinations were entirely negative. X-ray examination showed an area of erosion in exactly the same position as in the preceding cases.

or by the application of cold to the head. During the past year, the patient had several attacks of weakness and numbness of the left arm and leg, but the motor power was never entirely lost.

The patient's head has been abnormally large since childhood, but has not grown in the past fifteen years. The large head suggested a spontaneously healed hydrocephalus.

The results of the physical, serologic, roentgenologic and neurologic examinations were negative. Two diagnoses were suggested: (1) a cerebellar lesion which might have been responsible for the old hydrocephalus and was now causing attacks affecting the left side of the body; (2) a neurosis. The patient was very introspective, and had always feared paralysis.

*Operation.*—A cerebellar exploration was made after ventricular estimation had shown large ventricles. An enormous occipital dural sinus 2.5 cm. in width was



Fig. 12.—Erosion of the bone by a venous aneurysm of the dura.

found and ligated (fig. 13). The cerebellar region was normal. The foramen of Magendie was as large as the circumference of a lead pencil. The patient's headaches persist unchanged five years after the operation. The occipital sinus therefore had no bearing on the causation of the headache.

#### ANGIOMAS

Luschka (1854), who described the first angioma of the brain, divided angiomas into two types: (1) those arising by sequestration of a small portion of the embryonic capillary vascular system; (2) "true tumor" formation from vascular tissue. His case was of the latter type—a true tumor. The first type corresponds to the vascular nevi or telangiectases of the skin.

the attack came on. The attacks became more frequent, averaging about two a month. Most of the convulsions occurred just after waking in the morning.

The results of the physical and neurologic examinations were entirely negative. There was no objective weakness of the right arm and leg. The roentgenogram showed a marked thinning of the inner table of the skull along the midsagittal line and about midway between the nasion andinion (fig. 12). The area of erosion was about 3 cm. long. There was a slight bulging of the outer table over this region.

The combination of this erosion of the skull and the focal attacks beginning in the leg suggested that the probable lesion was a venous aneurysm—diverticulum of the longitudinal sinus.

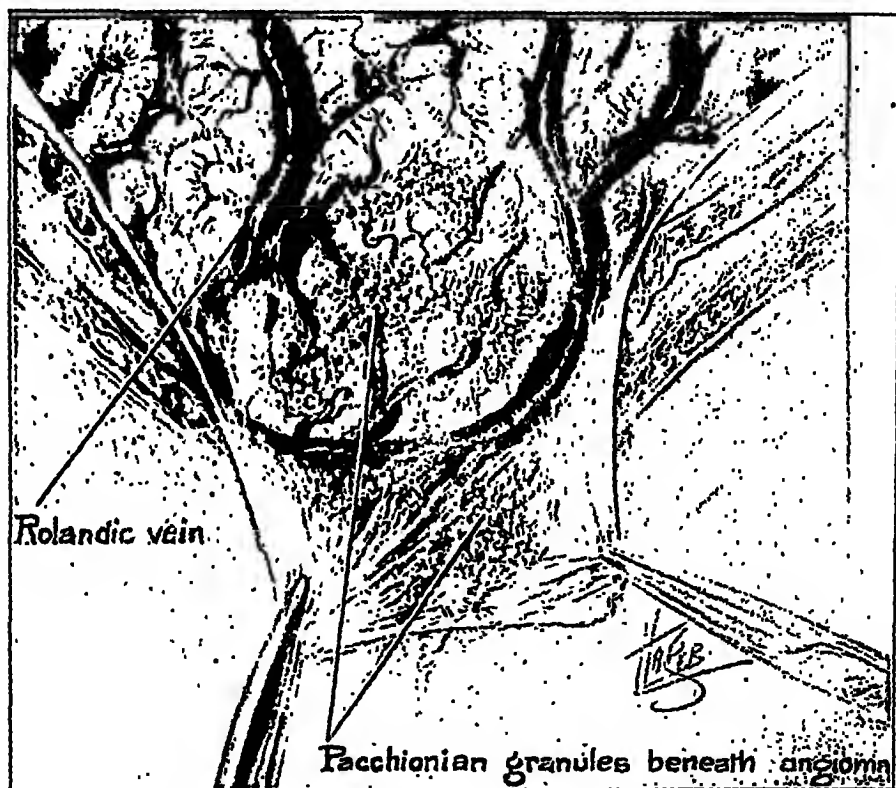


Fig. 11.—Sketch made at operation to show the effect of the dural venous aneurysm on the brain. The under surface of the dura is attached to the brain by a mass of pacchionian granulations.

*Operation.*—Precisely the same operation was performed and the same observations were disclosed as in the first case of this group.

The immediate postoperative recovery was uneventful. The operation was performed only a month before this paper was written.

#### CASE 11.—*Abnormality of Occipital Sinus.*

A well nourished man, aged 34, was referred by Dr. W. S. Thayer because of headaches in the occipital region. Throughout boyhood, the patient had had periodical headaches, always localized to the back of the head, at times radiating to the eyes. The headaches had increased with age. They were always intensified by work or exercise, and improved when the patient was in a recumbent position



a review of the literature on angiomas of the brain, I did not see any reference to similar observations, unless the case of D'Arcy Power is of this type. From the brief note and the accompanying sketch, this appears unlikely; more probably the tumor in Power's case was an arteriovenous aneurysm.

There seems to be no reason why a venous plexus should occur in the spinal cord and not in the brain. In the present series of angiomas of the brain, there are four examples of this lesion. A remarkable example of bilaterally symmetrical venous plexuses in the sylvian fossae is shown in case 7 (figs. 7, 8 and 9), reported under venous anomalies. In addition, there are several smaller circumscribed plexuses over both cerebral hemispheres. This patient was only  $2\frac{1}{2}$  years old, and since the vascular lesions were accompanied by other congenital cerebral defects, it is fair to conclude that the angiomas were of congenital origin also. Cases 2 and 6 (figs. 2 and 6) of the venous anomalies are also examples of this lesion, although in case 2 the form was perhaps less pure, since numerous large veins ran into the plexus, making it less sharply defined. These three cases show how insensibly venous anomalies and venous angiomas of this type blend into each other. In a final analysis they are probably identical.

A fourth example (case 12, fig. 14) of this lesion is presented with reservations, since the entire extent of the lesion was not seen. Although the tumor displayed the exact gross appearance of an angioma of the venous plexus type, it is not impossible that an underlying solid tumor may have been beyond operative exposure. Although solid tumors may cause a plexiform assembly of veins, it seems incredible that one so extensive could arise from this source. At the time of the operation, an extensive exposure was made in search of a solid growth. This patient was the only one of the series who was an adult. His symptoms were those of a slowly growing tumor in the hypophyseal region. The sella turcica was destroyed; there was at first bitemporal hemianopsia and later primary atrophy of one optic nerve with retention of vision only in the nasal half of the other eye. There was also, in addition, pain in the trigeminal domain on both sides, probably explainable by the overflow of the angioma laterally. In retrospect, it is difficult to see how the character of the lesion could have been determined from signs and symptoms. One should still have had to be content with the pre-operative diagnosis of a hypophyseal tumor.

There has not been any occasion to remove a venous plexus of the brain. In one patient (case 7), it appeared to have no bearing on the hydrocephalus, for which relief was sought. Should one be more favorably situated over the cerebral cortex and at the same time be more circumscribed, it should not be difficult to remove. I have removed completely four of these from the dorsal side of the spinal cord, with

Before Luschka's report, tumors of both types were well known elsewhere in the body, and because of their cavernous structure Rokitan-sky referred to them as "cavernous angiomas," a name by which they have since been known. It is questionable whether this classification is pertinent at the present time. There is, it is true, the type in which there is little connective tissue between the vascular spaces, and another type in which the connective tissue predominates and the vascular spaces are of microscopic size; but there seems little, if any, fundamental difference between the two types. Certainly both types grow like tumors. Whether one arises *de novo* and the other is always of congenital origin has not been proved. At the present time it seems prefer-

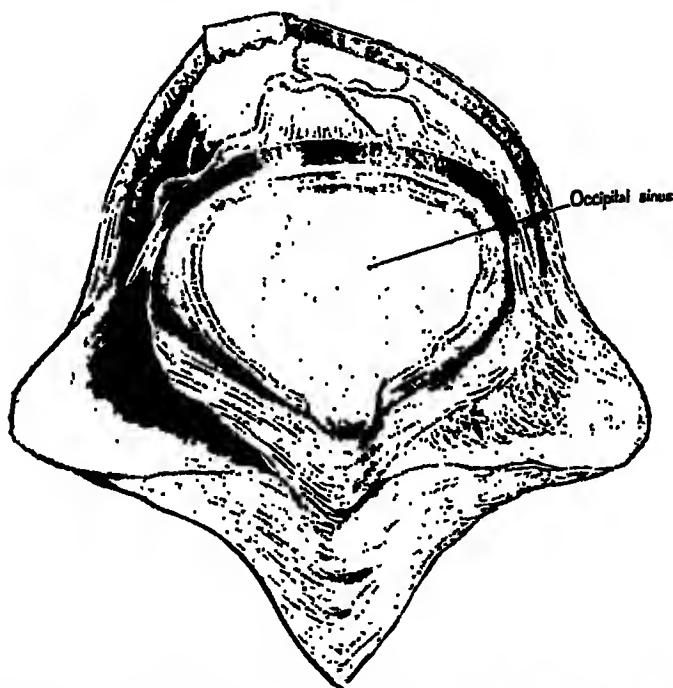


Fig. 13 (case 11).—Operative sketch of an occipital sinus of tremendous size. It is a congenital venous anomaly.

able to avoid classification based on conceptions of origin and to group them all as cavernous angiomas. When the stroma is in abundance and the vascular spaces microscopic, this type of angioma is frequently known as hemangiomendothelioma or perithelioma. In addition to cavernous angiomas, there is another type which should be added—venous plexus or angioma plexiforme.

#### ANGIOMA PLEXIFORME

A lesion of this character has been described among tumors of the spinal cord, where they are not uncommon. In a series of seventy-five tumors of the spinal cord, I had four angiomas of this character. In

operation, presumably from restriction of morphine, though possibly from an extradural hemorrhage. He was conscious until shortly before death. Necropsy was not permitted, so that further observations on the origin and distribution of the angioma cannot be added to the operative notes.

### CYST WITH ANGIOMA IN THE WALL

Of all the tumors of the vascular system of the brain, angiomatous cysts offer the best prognosis. It may almost be said that as a type and eliminating individual exceptions, they offer more than any other tumor of the brain. Usually the cyst is large and the tumor small. The

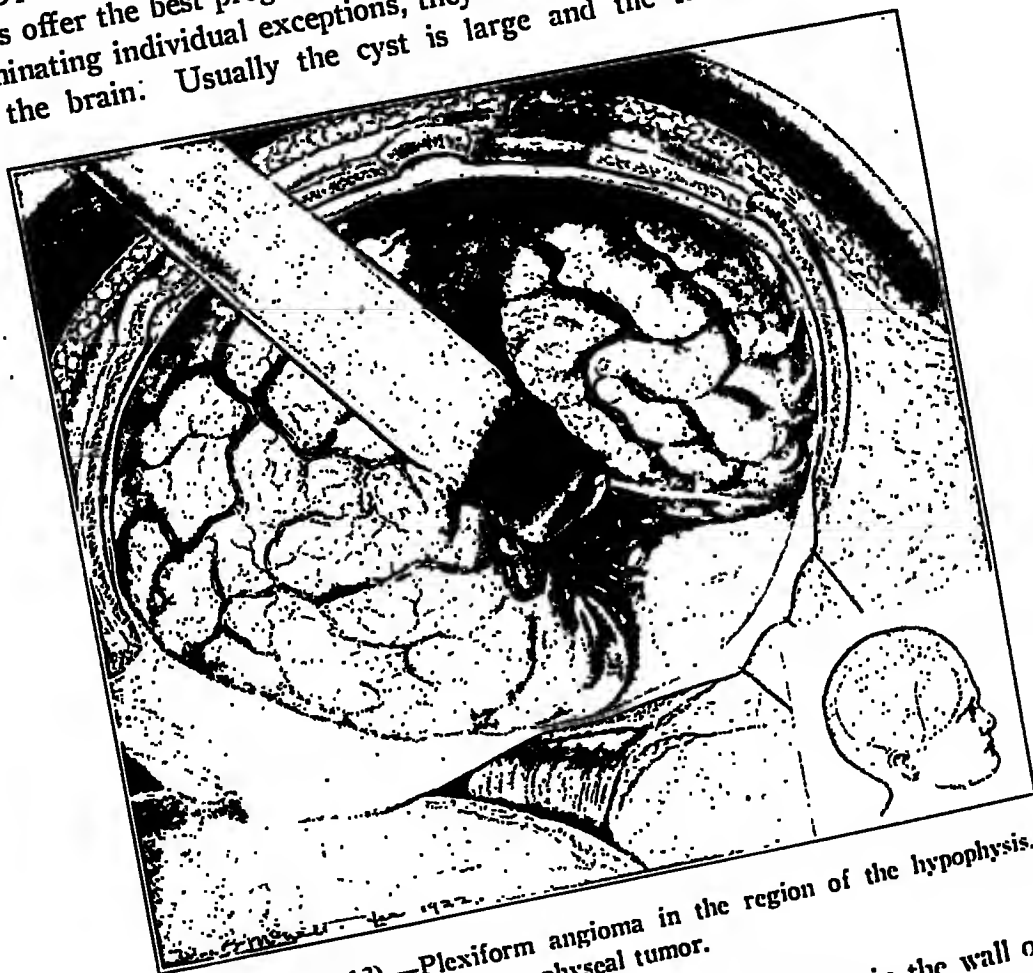


Fig. 14 (case 12).—Plexiform angioma in the region of the hypophysis. It caused all the symptoms of a hypophyseal tumor.

tumor is embedded in and projects from some point in the wall of the cyst. Always relatively small, compared to other tumors, it may actually be so small as to escape casual observation. There can be no doubt that in many of the so-called simple cysts a tiny angioma will be found on more careful inspection. The solid tumor is flat or rounded; it varies in size from a few millimeters to 2 or 3 cm. in diameter. Its surface is smooth and appears to be covered by the smooth lining of the cyst, but the cyst is not lined with epithelium. On sectioning the wall, a minute, insignificant looking, reddish brown lesion will frequently be

only one death, which occurred several days later from meningitis. Although the hemorrhage might at first appear to be a formidable danger, there is actually little to be feared. The loops of veins are bound loosely with arachnoid connective tissue, and when carefully separated, the whole network of venous loops becomes disengaged, much like a skein of yarn, and becomes resolved into two or three long veins which communicate with each other and with other veins on the surface of the cord. In the case which came to necropsy, the venous channels had entered into the spinal cord. The venous spaces within the spinal cord occupied a considerable volume of the cord and probably accounted for the symptoms more than did the great plexus of vessels on the surface.

#### REPORT OF CASES OF ANGIOMA PLEXIFORME

##### CASE 12.—*Angioma Plexiforme.*

A physician, aged 44, was referred by Dr. Carl Henning of Washington with the diagnosis of a hypophyseal tumor. His chief complaints were continuous ocular neuralgia and bitemporal hemianopsia. He had always had headaches. Due to severe paroxysms of pain in the eyes, he had become a morphine addict, finally taking from 10 to 12 grains (0.65 to 0.78 Gm.) a day. The addiction to morphine dated back six years, when the pains had become unbearable. Only through the use of this drug was he able to keep at his work. The pain first began in the right eye and often radiated to the cheek and teeth on the right side. Two years before admission to the hospital, diplopia had appeared and had been present at varying intervals until this report was written. At that time, an x-ray examination showed erosion of the posterior clinoid processes. Two years before, pains of the same character had extended to the left eye, face and teeth. A bilateral temporal hemianopsia had then been found by Dr. Henning. Teeth on both sides had been extracted, at patient's insistence, in an effort to get relief from the pain. Eighteen months before, a subtemporal decompression had been performed elsewhere, but without appreciable benefit.

Neurologic examination revealed the following: 1. A bitemporal hemianopsia was noted which was not sharply demarcated, there being some slight vision in the temporal fields near the center. The visual acuity was greatly reduced, more in the right eye, with which fingers could not be counted at a distance of 20 cm. 2. There was the characteristic pallor of primary atrophy in the temporal side of both disks. The nasal margin of each disk was hazy. The retinal veins were moderately engorged and tortuous. 3. There was complete destruction of the posterior clinoid processes (x-ray examination); the sella turcica was deep. Otherwise, the results of the examination were negative. There was no objective, sensory or motor disturbance referable to either trigeminal nerve. The Wassermann reaction of the blood was negative.

*Operation.*—In March, 1922, an anterior right craniotomy was performed for exploration of the hypophyseal region. A bluish tumor protruded anteriorly between the optic nerves (fig. 14). When the arachnoid membrane was opened and the cerebrospinal fluid allowed to escape, the tumor was seen to be a mass of entwined veins, each about as large as a slate pencil. Pulsation could not be observed. There was no evidence of arterial blood such as one sees through the wall of distended veins in an arteriovenous aneurysm. Treatment of the lesion being hopeless, the wound was closed. The patient died thirty-six hours after

angioma. Moreover, even with a hematoxylin eosin stain, the reticulated stroma of a glioma has little resemblance to that of an angioma.

Lindau's intensive study demonstrates anew the fact that when supposedly rare lesions are better known they are frequently found to be common. All seven of my cases of intracystic angiomas were in the cerebellum. As indicated in the accompanying sketches, the solid tumors were located at divergent parts of the wall of the cyst. All have reached the surface of the cerebellum and have been in contact with the pial vessels, but whether this is significant in their origin, I am not prepared to suggest.

*Clinical Features.*—There is nothing characteristic about the signs and symptoms produced by angiomatous cysts. Other types of cysts in the same position and of the same size give identically the same disturbances. All produce intracranial pressure, usually but not invariably evidenced by headache, nausea, vomiting and papilledema; they therefore compromise life. In most instances they also induce symptoms of localization, but this is not always true. If the cyst occupies a silent area of the cerebral hemisphere, localizing symptoms will be absent until it has grown alongside cerebral tracts with function—speech, motor, sensory, visual, uncinat, etc. All of the cases of cerebellar cysts collected from the literature showed outspoken so-called cerebellar disturbances—staggering gait, often with the tendency to swerve to one side, positive Romberg sign, and often nystagmus, ataxia, adiadokokinesis, stiffness of the neck and dizziness. One of my patients did not have any symptoms or signs of localizing import. Another had symptoms which were suggestive, but not positive. In these cases, ventriculography and ventricular estimation made the location absolute.

Clonic convulsions probably never occur with cerebellar cysts, but frequently with cerebral cysts. Convulsions resulting from cerebral cysts are often of focal character and may have the jacksonian characteristics. In the cerebral cases reported, in those of Schweyer, Bruns and Baum the patients had jacksonian seizures; Bielschowsky's patient alone did not have convulsions. None of the twenty-four cerebellar cysts produced clonic convulsions. On the other hand, tonic spasms may occur in the late stages of cerebellar cysts. Such attacks are, in fact, characteristic of a tumor in the posterior cranial fossa; they result from compression of the motor tracts in the brain stem. This phenomenon was seen in cases 14 and 15. Newmark's patient had momentary losses of consciousness without convulsions.

Although a genuine hemiplegia or hemianesthesia is usually referable to lesions of the cerebral hemisphere, a few of the cerebellar angiomatous cysts induced paralyses, though usually in transient attacks. One of Lindau's patients had attacks in which both legs were paralyzed; another lost the use of the left arm and leg at times. Two of my patients had

found to cause the relatively enormous cyst. In the gross appearance, the intracystic angiomas are usually mistaken for gliomas. A careful gross inspection will usually make the differential diagnosis. An angioma is fibrous and acellular and the larger tumors are usually compressible and spongelike. In the fixed specimen, the tumor has changed from reddish brown to black, because of the old fixed blood in the tumor. A glioma is softer, more cellular and consequently more friable. Cells of the latter easily scrape off on the edge of a scalpel. It is noncompressible and its color a more uniform brown in the fresh specimen and a less intense brown or black when fixed. The content of cysts, whether of angiomatous or of gliomatous origin, is apparently the same. In either type, the fluid is clear lemon or orange yellow and a white coagulum is present at the bottom of the cyst. The reason for the cyst formation in these tumors is not known.

In an intensive study of cysts of the cerebellum, Lindau assembled fifteen cases, including a case reported previously by Schloffer, and another by Friedrich and Stiehler. This number is many more than the combined total number of all the cases, both cerebral and cerebellar, in the literature.

Other cases of angiomatous cysts were reported by Luzzatto, Bielschowsky, Baum, Bruns, Koch, Newmark and Schweyer. Four of these (Bielschowsky, Baum, Bruns and Schweyer) were in the cerebral hemispheres; two in the cerebellum and one (Luzzatto) in the brain stem. Koch's patient had bilateral angiomas. In Newmark's case, the tumor was in the meninges and the cyst was extracerebellar. Including my seven cases, there have now been reported twenty-nine cases of angiomatous cysts, twenty-four cerebellar, four cerebral, and one in the brain stem.

It is of interest to note that Lindau found angiomatous cysts to be almost twice as frequent as those of gliomatous origin. He doubtless refers to the large cysts with small single intracystic papilloma. Lindau's statements are supported by careful histologic studies with differential stains to detect glia fibers. From operative experience, the histologic evidence indicates the angiomatous and gliomatous cysts to be about equally divided. However, there are three cases diagnosed gliomatous cysts which I feel confident, because of the gross description in the operative notes, are angiomatous cysts; the sections have been lost. If these are really angiomatous cysts, the results would be similar to those of Lindau. On a restudy of the histologic material, it is surprising to find how many tumors have previously been diagnosed gliomas when they are sharply defined angiomas. There are many exceedingly vascular gliomas which in the gross or microscopic examinations might be mistaken for angiomas, but a careful study of the vascular spaces of a glioma show well defined vascular coats which are absent in the

absence of profound disturbances of a primary lesion of the brain stem a cyst, angiomatous or gliomatous, should be suspected.

*Treatment of Patients with Angiomatic Cysts.*—Angiomatic cysts are usually among the easiest and safest intracranial lesions to extirpate. Extirpation of the little tumor embedded in the wall of the cyst is sufficient. The extirpation must be done painstakingly, and a good margin of tissue must be included with the angioma. The danger is minimal when the tumor is small and situated near the surface. It increases somewhat when the tumor is larger and is located far forward over the midbrain. The larger tumors are usually vascular and for this reason offer difficulties in removal. A most important factor in the safety of the operation lies in the early diagnosis. In the late stages, the subtentorial pressure is so high that the dura cannot be safely opened because the cerebellum will herniate through the dural defect and rupture. Puncture of a lateral ventricle will relieve the supratentorial pressure, but not enough to prevent injury to the cerebellum. Puncture of a cerebellar lobe with a hollow, blunt needle will eliminate this hazard when a cyst is reached.

It is hardly necessary to add that as methods of treatment in an effort to cure tapping or completely evacuating a cyst by a transcortical incision, or treatment of the tumor by Zenker's solution or some other fixative are perfectly futile. They are inexcusable, for they have left uncured a lesion which can be so easily removed and permanently cured.

The operative efforts reported in the cases compiled from the literature have not been numerous. The first extirpation of a tumor of this type was performed by Bruns in 1897, but his patient died of meningitis. Baum's (1911) patient was in coma at the time of the operation, recovered, and died a year later of pneumonia. Schloffer's (1926) patient recovered after an extensive resection of a cerebellar hemisphere. One of my patients died nearly ten years ago, without exposure of the tumor. At that time there was no means of locating the tumor (she was in deep coma at the time) and the then routine subtemporal decompression was performed, of course, without relief. From careful inspection of the autopsy specimen, it is doubtful whether at that time the cyst could have been found for there was no surface evidence of its presence when the brain was removed. The tumor was 4 cm. beneath the surface of the cerebellum. I have also wondered whether the solid part of the tumor would have been detected had it been possible to locate and open the cyst. At the present time, however, the methods of accurate localization of tumors would make the disclosure of the cyst possible regardless of its depth. The five patients on whom the extirpation of the tumor in the wall of the cyst has been performed have made uneventful and complete recoveries and are now living and well. They are without any signs of recurrence of the tumor. One patient is well seven years

attacks of pain and numbness in one side of the body (cases 13 and 18). One of Lindan's patients and one of mine had trigeminal pain; in both instances the cerebellar cysts were unilateral. Luzzatto's case of a cyst in the medulla gave symptoms suggesting syringomyelia, and in its gross appearance the cystic cavity was like that found in syringomyelia. Recently several cases of syringomyelia with cysts of the spinal cord have been reported in which tiny angiomas have been secreted in the walls of the cysts.

The reflexes are altered according to the relationship of the tumor to and the degree of injury of the motor tracts. Among the cerebellar cysts, reflex changes are usually not great, though not infrequently ankle clonus, a positive Babinski reflex and increased deep reflexes are present on one or both sides—constantly or transiently. The corneal reflex is frequently diminished and at times absent on the side of the unilateral tumor and on both sides from a midline tumor of the cerebellum.

The age at which symptoms first appear is essentially the age of greatest frequency of tumors of the brain in general, i.e., between the ages of 25 and 50.

The time of the initial symptoms in eighteen cases of cerebellar angiomatous cysts is as follows: between the ages of 20 and 30, three cases; between 30 and 40, nine cases; between 40 and 50, four cases; between 50 and 60, two cases.

In half of all the cases, symptoms first appeared in the third decade. The youngest patient was 21, the oldest, 52 years.

The duration of symptoms before death or operation is surprisingly short in most cases of cerebellar cysts. In six, the symptoms had been present less than six months; in four, less than one year or more than six months; in four, two years or less; and in one each, three, four, five and eight years. In approximately half of the cases, therefore, the symptoms began less than one year before death or operation. Only two cerebral angiomatous cysts have data concerning the duration of symptoms: Bielschowsky's patient had symptoms for fourteen months and Schweyer's for twelve years. It is obvious that the rapid onset of symptoms is due, not to the size of the comparatively insignificant tumor, but to the growth of the cyst which forms with relatively great rapidity.

Four of my patients were males and three were females. From the cases in the literature there are more males, fifteen to eleven. The frequency is probably not influenced by sex.

By using this analysis of signs and symptoms, it appears possible to make at least a tentative diagnosis of an angiomatous cyst—an absolute diagnosis seems impossible. Given a cerebellar tumor appearing in a patient between the ages of 25 and 40, symptoms rapidly progressive (less than one year) with variations in them from time to time and th-



One month before admission to the hospital, her vision suddenly had become blurred and since that time she had been blind. Attacks of nausea and vomiting had been present for the past three months. It is of interest that two years ago an ovarian tumor, said to be a carcinoma, had been removed by Dr. Terry in San Francisco.

Neurologic examination elicited the following positive observations: 1. There were tremendous bilateral choked disk (6 diopters); each nerve head was covered with dozens of hemorrhages. Much of the contiguous retina was also obscured by the hemorrhages. 2. The patient could not see fingers with either eye. 3. She showed a positive Romberg sign and fell to the right. 4. Staggering gait and

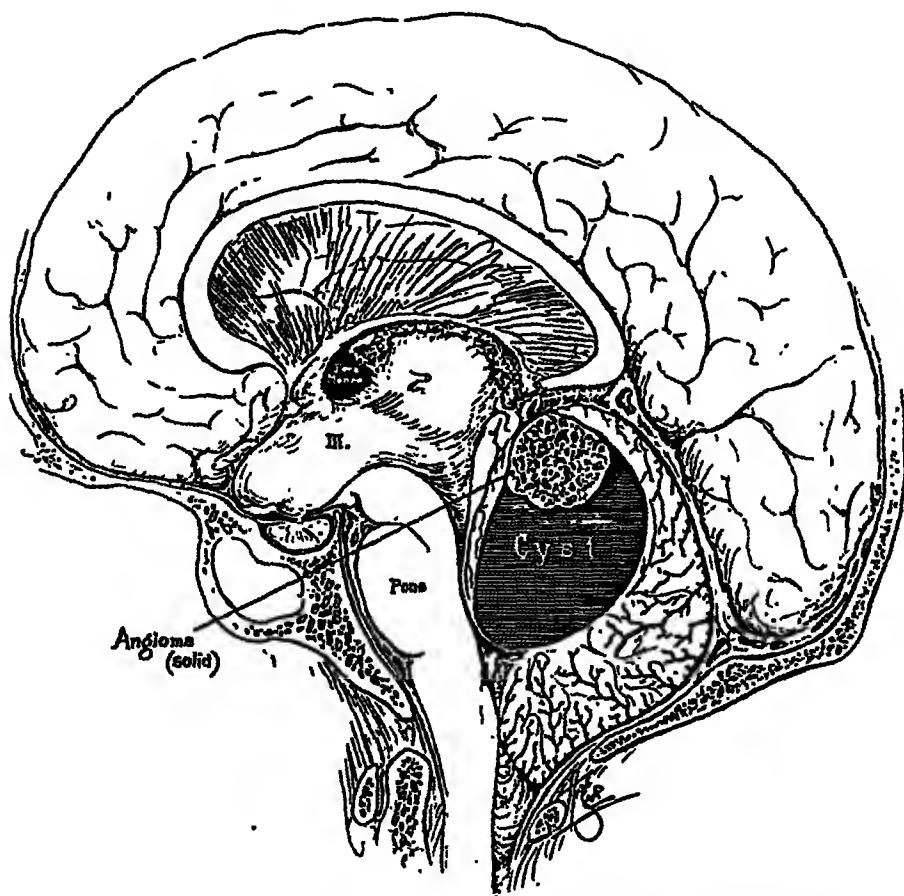


Fig. 15 (case 13).—The operative observations in an angiomatous cyst. The solid tumor was situated directly over the midbrain.

5. Hyperactive but symmetrical reflexes were present. The Wassermann reaction of the blood was negative. X-ray examination of the head was negative. A metastatic tumor was suspected.

Ventricular estimation (at time of operation) showed that the lateral ventricles were large and communicated freely with each other (indigo carmine test). The pressure of the ventricular fluid was very high.

*Operation.*—On Jan. 6, 1923, cerebellar exploration was performed. A large cyst was struck with a hollow needle 3 cm. below the surface of the vermis (fig. 15). A transverse transcortical incision was then carried into the cyst, which was larger than a walnut. Straw colored fluid escaped, and a gelatinous coagulum

after operation (April 13, 1921). At the time of the operation, he was in deep coma. The operation was performed only after the tumor was localized by ventriculography. Another patient is well after five years. Her vision, which was lost due to retinal hemorrhages caused by the intracranial pressure, has returned to normal. Another patient who was nearly comatose quickly became conscious after operation (sixteen months ago).

The seventh patient died en route to the hospital, though in good condition when he left home. The sudden development of coma, and the comparatively short duration of the intracranial signs and symptoms, make an early diagnosis of paramount importance, if cures are to be obtained. Often warning is not given that death impends.

The only safe way to relieve intracranial pressure due to a cerebellar cyst is to evacuate the cyst. The relief is then prompt and complete for the time being; it becomes permanent when the tumor—the cause of the cyst—is removed. The evacuation of the cyst relieves not only the direct pressure on the brain stem, but also the hydrocephalus. Relief of the latter is almost as important as the former, for the hydrocephalic ventricles gradually push the tentorium backward and exert great pressure on the structures—including the medulla—in the posterior cranial fossa. A subtemporal decompression does not effect relief in the slightest degree. A subtentorial decompression may or may not effect temporary relief depending on whether the tumor can be lifted from the foramina of Luschka. The only safe and certain attack therefore is to open the cyst and extirpate the tumor. This same principle of relief by the direct operative attack on tumors holds true for all intracranial neoplasms. There could not be better proof of this statement than the prompt recovery from coma after removal of the cause of the intracranial pressure in the foregoing cases.

#### REPORT OF CASES OF CYST WITH ANGIOMA IN THE WALL

##### CASE 13.—*Angiomatous Cyst.*

A well nourished woman, aged 32, blind and unable to stand, was referred by Dr. George Price of Spokane, Wash. Her symptoms dated back only seven months, when she had noticed stablike pains in both eyes which had lasted only a few seconds and had disappeared when she lay down. There was also some headache in the frontal region and sides of the head. They had become more severe and more persistent; for the two months prior to operation they were constant.

Sudden fainting spells, lasting from ten to fifteen minutes, and without loss of consciousness, had occurred nearly once a week for the past five months before operation. She felt dizzy during these spells; her "thoughts were paralyzed" and "everything seemed to rush to the head" and she would fall to the floor. Staggering gait had been present two months; she swayed from side to side and had a tendency to bear to the right. She had had occasional attacks of numbness of the right arm and leg, and the neck had been rigid.

tonsil which had herniated into the foramen magnum. It was necessary to liberate the tonsil in order to reach the tumor and permit its extirpation. The tumor was excised with a zone of normal cerebellar tissue on all sides. Histologically, the tumor was a typical cavernous angioma.

The patient made a complete recovery and is now well. There are no residual cerebellar symptoms.

CASE 15.—*Angiomatous Cyst.*

A well nourished woman, aged 44, entered the hospital in coma, in October, 1918. For two months she had complained of dizziness after exertion, and some suboccipital headaches associated with vomiting nearly every day. At first, when perfectly quiet she had been comparatively free from both headache and dizziness, but gradually the headaches had become much more intense and were not affected by resting. She staggered like a drunken person and had shaking of both hands (but more the right), so that at times she was scarcely able to lift the cup to her mouth. She had several attacks in which her whole body became rigid like a board, but consciousness was not lost nor were there any clonic convulsive movements. A month prior to operation, she had had periods of mental cloudiness, some hallucinations and had been disoriented. Later she had alternately laughed and cried and had ceased to take interest in her surroundings.

The physical and neurologic examination showed the following:

A coarse tremor of the right hand and arm was frequently observed. The veins of the forehead and eyelids were very full. The eyegrounds showed fullness of the veins and a beginning bilateral papilledema. The Babinski reflex was positive on both sides; the corneal reflex and knee jerks were normal, and ankle clonus was not noted.

At the time this patient was seen, the stereotyped treatment for such patients was a subtemporal decompression—now known to be useless. Through the operative defect a large lateral ventricle was tapped, reducing the supratentorial pressure to normal. She died twenty-four hours after the operation.

When the brain was examined at necropsy, evidence of the tumor was not found on the surface of the brain. Section of the cerebellum, at a later date, showed a cyst about 3 by 3 cm. in diameter. At first evidence of a solid tumor was not present, but later a small circular thickened area about 3 mm. in diameter was detected. Microscopic examination of this area showed a typical angioma.

CASE 16.—*Angiomatous Cyst.*

A young engineer, aged 28, was seen, in consultation with Drs. Julius and Harry Friedenwald of Baltimore, at another hospital on April 13, 1921. He was then comatose despite a subtemporal decompression which had been performed two weeks before.

The following history was obtained from Dr. Friedenwald: The symptom of onset was an attack of headache, lasting three or four hours, and beginning six months before admission to the hospital. At first, the attack recurred about every ten days, but for the three months before admission they had been continuous and frequently associated with nausea and vomiting. For three months he had been troubled with dizziness and staggering gait. The dizziness was always worse when he was lying on the right side. Diplopia had been present at times for three or four months.

The results of the neurologic examination were negative, except for a bilateral papilledema of high grade. The decompression in the right subtemporal region was full and tight.

*Operation.*—On April 13, 1921, an injection of air was made: the tumor was localized to the posterior cranial fossa, and a cerebellar operation was performed.

was removed. A small, rounded, firm papilloma about the size of a hazelnut projected from the wall of the cyst at its anteriormost part and lay just under the great vein of Galen. Its removal was attended by such profuse bleeding that its angiomatic character was at once apparent. Though its base was only about 0.75 by 0.75 cm., every attempt to dissect it free was followed by a brisk hemorrhage. After it was removed the bleeding surface was temporarily packed with moist cotton under pressure, and later the use of silver clips completely stopped the bleeding. The unopened fourth ventricle bulged into the floor of the cyst.

Microscopic examination showed that the tumor was made up of endothelial lined, blood-containing spaces of varying size. Abundant connective tissue interposed between the vascular sinuses was the only other feature of the tumor.

The patient made an uneventful recovery. Five years later, she was well; her vision had returned; her gait was unaffected, and she was able to do her own housework.

#### CASE 14.—*Angiomatic Cyst.*

A poorly nourished woman, aged 36, was referred by Dr. F. H. Kliefoth, of Schertz, Tex., on Feb. 20, 1928. Six months before, suboccipital headaches had first appeared with nausea and vomiting. Dizziness and staggering gait, dimness



Fig. 16 (case 14).—Small mass of cerebellar tissue removed with the angioma. The light part of the picture is cerebellar tissue; the dark area is the angioma.

of vision and diplopia had soon developed and had increased. Later, the patient had been subject to "nervous spells" in which numbness extended upward from the fingers and toes of both sides. During these spells, which lasted from twenty to thirty minutes, the arms were flexed, the legs extended and she was unable to move. Until the attack passed, she was unable to speak, although she was conscious.

Examination showed an extremely ill woman. She was drowsy in spite of the severe headaches to which she had been subject. It was evident that she was bordering on coma.

The Romberg sign was positive; she promptly fell to the left; ataxia and adiadokokinesia were positive on the left; there was lateral nystagmus. High grade papilledema of both eyegrounds was observed.

*Operation.*—The diagnosis of a cerebellar tumor was confirmed by ventricular estimation, and a bilateral cerebellar exploration made. A cyst of the left cerebellar lobe was found and evacuated (fig. 16). The cyst was about as large as a walnut, and contained clear orange-yellow fluid. The fourth ventricle bulged into the mesial side of the cyst. A small smooth reddish-brown tumor, about as large as a split pea, could be seen in the wall of the cyst; it was located in the left cerebellar

abrupt vertical line was reached 2 cm. back of the aqueduct (fig. 17). This line marked the anteriormost part of the tumor.

*Operation.*—On Nov. 2, 1927, a bilateral cerebellar exposure was made. The bone was exceedingly bloody, despite the release of pressure by a ventricular puncture. The dura was still so tight that it seemed unsafe to expose the cerebellum. Puncture of the left and right cerebellar lobes yielded nothing; on puncturing the vermis, a yellow fluid spurted. With the dural tension relieved, the dura was evacuated. A colorless, gelatinous clot was pulled out of the bottom of the cyst. The outer surface of the cyst contained only meninges, the cortex having been entirely atrophied. The cerebellar tonsils were herniated far into the spinal canal. After the cyst was evacuated, the tonsils could readily be with-



Fig. 17 (case 18).—Ventriculogram showing the localization of an angiomaticous cyst which did not give signs or symptoms by which its position could be identified. The wide aqueduct of Sylvius and the anterior part of the fourth ventricle are between the two sets of arrows. The tumor produced an abrupt ending of this ventricular shadow.

drawn from their incarcerated position; as they were withdrawn, one could see a cluster of little yellowish cystic nodules much like a bunch of grapes. They occurred as much in one tonsil as in the other. They were attached to the meninges. The fourth ventricle bulged into the cyst. The anterior part of the solid tumor was attached to the wall of the cyst, where it was inseparable from the fourth ventricle. The entire solid tumor was removed with a good margin of cerebellar tissue. This procedure necessitated the removal of both tonsils and part of the roof of the fourth ventricle. The tumor and brain tissue weighed 9 Gm.

A large cyst of the left lobe was first tapped, then evacuated through a transcortical incision. Clear, yellowish fluid escaped from the cyst. On the posterior lateral wall of the cyst was a smooth, reddish-brown solid tumor about as large as a pea. It reached the surface of the cerebellum. The solid tumor was removed with a zone of normal cerebellar tissue.

Recovery was prompt and complete. The patient has since carried on his occupation and has remained entirely well.

**CASE 17.—*Angiomatous Cyst.***

A poorly nourished man, aged 35, was referred with the diagnosis of a tumor of the brain on June 3, 1924. His symptoms dated back only three months, when he had suddenly been seized with a severe occipital headache, dizziness and vomiting. The attack had lasted two days. Similar attacks had recurred with increasing frequency. Three weeks after the onset of his illness, staggering gait had developed. Vomiting had become so intense that he lost 30 pounds (13.6 Kg.) in weight. Occasionally, there had been roaring in the right ear. From time to time, dark spots had appeared before the eyes, and for six weeks before operation his vision had been blurred. He had been bedfast for four weeks fearful of turning his head because of the certainty of precipitating dizziness. Diplopia had not been present.

**Neurologic Examination.**—The patient could only see enough to count fingers. There was a marked papilledema of both optic nerves. Many hemorrhages obscured the region of the disks. There was a positive Romberg sign, with tendency to fall to the left and backward; retropulsion, unsteady gait, cervical rigidity and ataxia were present. The reflexes were normal. A Babinski reflex or ankle clonus was not noted.

**Operation.**—On June 4, 1924, ventricular estimation showed marked hydrocephalus, with free communication between the lateral ventricles—indigo carmine passed quickly from one ventricle to the other.

Because of the patient's poor physical condition, the operation was performed under local anesthesia. A large cerebellar cyst was tapped in the left lobe; clear lemon-yellow fluid escaped. A smooth, reddish tumor, as large as a cherry, protruded slightly into the cavity of the cyst at the outer aspect near the midline. It also penetrated through the remaining cerebellar tissue to reach the surface. The tumor was easily excised with contiguous cerebellar tissue. The patient made an uneventful recovery, and has since been well (nearly four years).

**CASE 18.—*Angiomatous Cyst.***

A large, strong man, aged 34, was referred by Dr. Malcolm Campbell, of Malvern, Ia., on Oct. 20, 1927, with the diagnosis of a tumor of the brain. His symptoms had begun two years before, when he had first noticed pain in and behind both eyes and radiating to the occipital region. Eighteen months later, severe occipital headaches had begun, and had persisted up to the time of operation. During the month before operation, he had had spells of numbness and tingling in the right arm and leg. Dizziness, vomiting or unsteadiness of gait were not noted.

The neurologic examination showed a bilateral papilledema measuring 5 diopters in each eye. There were no other positive neurologic observations. The Romberg sign was negative; ataxia, or nystagmus was not noted. There were no signs by which the localization of the tumor could be made.

Ventriculography showed that the lateral ventricles were much enlarged; they communicated freely; the third ventricle was enlarged and mesially placed; the aqueduct of Sylvius was patent throughout and also the fourth ventricle until an

Necropsy showed a large cyst of the left cerebellar lobe with a small flat circumscribed tumor embedded in the cerebellum and wall of the cyst (fig. 19).

Microscopically, the tumor was a typical cavernous angioma.

#### CAVERNOUS ANGIOMA

Cavernous angiomas differ from the foregoing group of tumors principally in the absence of a cyst and in the larger size of the vascular spaces which are usually on the range of unaided vision. The five cases here reported differ greatly from each other in the gross appearance of the tumors. On one extreme, they seem to fuse insensibly with the angiomas associated with cysts, and on the other with the plexiform angiomas. In general, it may be added that they lack the hyperplastic character of the former and the gross venous make-up of the latter.



Fig. 19 (case 19).—Angioma in wall of cyst of cerebellum. Some of the larger vascular spaces are visible. The tumor is well circumscribed but not encapsulated. This patient died en route to the hospital.

The tumor in case 20 showed a gross cavernous character, and in case 23, hyperplastic stroma. It has already been noted that the angioma plexiforme fused insensibly with the venous anomalies. It would seem therefore, that other types of lesions of the venous and capillary systems blend with each other. Perhaps it may be preferable to subdivide the cavernous angiomas into two types according to the early proposal of Luschka, but for the present I am inclined to disregard the differences and group them all together. Although many of the lesions of both the embryonal vascular type and of the angioplastic type (the so-called "true tumor" of Luschka) are small and apparently dormant, others with seemingly the same histologic and gross appearance are undoubtedly growing. Either, therefore, may or may not act as a neoplasm. Prolif-

The postoperative course was uneventful. The patient is now well (six months after the operation).

CASE 19.—A man of about 40 years of age was referred by Dr. R. R. Snowden, of Pittsburgh, with the diagnosis of an unlocalized tumor of the brain. For about a year he had been having headaches, which had gradually increased in intensity.

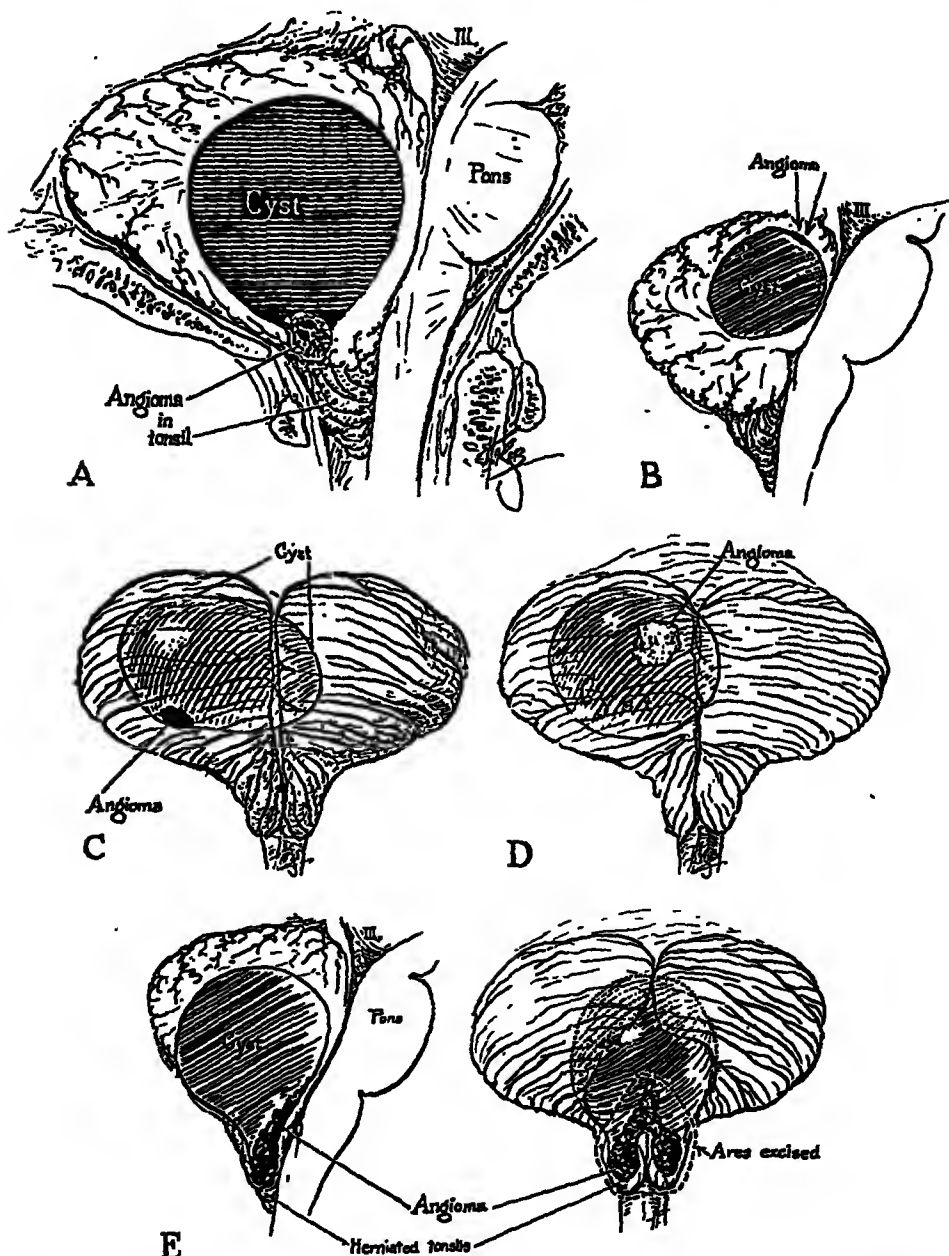


Fig. 18.—Sketches showing the location of the small solid tumors in a series of cysts: (a) case 14; (b) case 15; (c) case 16; (d) case 17, and (e) case 18.

For a few months prior to death they had been almost continuous. He had loss of vision, hiccups, projectile vomiting and inability to maintain his balance. With the exception of a double papilledema, Dr. Snowden did not make any positive observations on examination.

The patient died en route from the station to the hospital.



with hematoxylin and eosin stains, from which the diagnosis is easily made on the grosser aspects of the histologic picture.

*Signs and Symptoms of Cavernous Angioma.*—There is a striking uniformity in the symptoms when viewed as a whole. Occasionally, as in Kufs' patient who died at the age of 81, symptoms were not present. Other patients did not show symptoms until one of the vascular spaces suddenly ruptured and the patient died of a cerebral hemorrhage. Three patients from the group died in this way. This is a far smaller proportion of deaths from hemorrhage than in the group of arterio-venous aneurysms, probably owing to the arterial pressure in the defective walls of the latter.

A spontaneous cerebral hemorrhage occurring during the period of youth and middle age in a person without hypertension must nearly always indicate an underlying tumor or aneurysm. Most instances of so-called spontaneous "subarachnoid hemorrhage" arise in this way. At times the lesion is so small that it may be overlooked, or the vascular break may be a tumor of the spinal cord as in Lorenz's case. It is not fair to make a final anatomic diagnosis of primary "arachnoid hemorrhage" unless the spinal cord has been searched for angiomas, for these tumors are common throughout the central nervous system. Cases of angiomas of the spinal cord have been reported by Gaupp, Hadlick, Berenbruch, Lorenz, Roman, Pinner, Tannenberg, Lindau and Ritter. For the literature on this subject, the reader is referred to the publication of Tannenberg and Ritter.

The accompanying tables show at least three striking differences between cavernous angiomas and angiomatous cysts. 1. Most of the symptoms of cavernous angiomas are focal, and few are of general intracranial pressure. 2. The duration of symptoms is much longer. 3. The symptoms begin at an earlier age. Assuredly, these generalizations have their exceptions.

The clinical disturbances obviously depend on the location of the tumor as well as on its character. Tumors in the brain stem cause the most profound loss of function and affect life long before tumors in the silent lobes of the cerebral hemispheres. The symptoms in some of the cases of cavernous angioma occurring in early life are of short duration because the children so affected soon die.

In one of my patients, a tremendous cavernous angioma was present at birth. An external portion resembled an occipital meningocele; an internal portion pushed the cerebellum far forward and caused hydrocephalus. This tumor developed early in embryonic life, for at birth it was larger than one's fist. It doubtless developed early also because both the dura and occipital bone were honeycombed with parts of the tumor which connected the nerves within and without the skull. Kalischer's patient had convulsions soon after birth and died when he

ably the most rapidly growing and much the largest tumor of my series was one of the primitive vascular—presumably the least active—type.

Until Lindau's publication, the overwhelming percentage of angiomas was cavernous. With the addition of his great number of angiomatous cysts, the latter have come to assume a less subordinate position. The cavernous angiomas are far less concentrated to one locality in the brain, in contrast to the favored cerebellar habitat of the angiomatous cysts.

Forty-four cases of cavernous angioma have been found in the literature. The number reaches forty-nine, with the addition of the five cases included in this report. In nine of these cases (18 per cent), multiple tumors of the same character were scattered throughout the brain. In most of them, there were two or three angiomas (Finkelnburg, Jakob, Malamud, Müller and Ohlmacher), but in Creite's case there were eight, in Kufs' twelve, and in Huebschman's thirty; in Kalischer's case, the brain was studded with angiomas.

The distribution of these tumors is as follows: frontoparietal lobes, thirty-two; brain stem and fourth ventricle, fourteen; cerebellum, eight; in depth of cerebral hemisphere and third ventricle, nine; occipital lobe two.<sup>2</sup>

The gross appearance of a typical cavernous angioma is characteristic. It is spongelike and compressible because of the large spaces which one can usually see with the naked eye. It is always well circumscribed, but never encapsulated; its color is reddish brown because of the contained blood. Some of the tumors are soft, others firm, depending on the size of the blood spaces and the amount of connective tissue. Although they have a good venous and arterial blood supply, neither is excessive, and neither is disproportionate to the other. When opened at operation, they bleed freely and in proportion to the size of the cavernous spaces and the entering arterial supply. The bleeding is principally venous, though on the confines of the tumor the arterial bleeding may give some trouble. The tumors do not pulsate. The size of these tumors varies from minute areas to a mass larger than one's fist. The largest tumor in my series occurred in a baby, 1 month old. It was both intracranial and extracranial. Both portions were directly continuous through numerous small defects in the bone and dura.

Microscopically, these tumors show endothelial lined blood spaces with scant or not supporting coats, with a minimal amount of connective tissue between the blood spaces.

Thrombosis and calcification, principally the former, frequently occur, but apparently to a far less extent than in an arteriovenous aneurysm. Lindau has stained the tumors with glial stains to exclude the diagnosis of a glioma. Microscopic studies have been made exclusively

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2. Where multiple tumors were present they have been entered in each location.

trauma and cerebral hemorrhage from vascular tumors was considered in the paper on arteriovenous aneurysms.

Two of my four cerebellar cavernous angiomas would easily have been tolerated in the cerebral hemispheres without symptoms of pressure. The other two were large. One had grown tightly into the brain stem. The changes in the reflexes in this group of tumors are usually of little help in making a diagnosis; the deep reflexes are increased along with motor disturbance; an ankle clonus and Babinski reflex are at times present, at other times absent. In midcerebellar tumors, bilateral reflex changes may be found.

TABLE 1.—*Analysis of Symptoms*

Author	Date of Publication	Age	Sex	Type of Angioma		Tumor		Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs at Symptom
				Cavernous	Small Solid Tumor with Cyst	Single	Multiple						
Dandy.....	1928	44	M	Plexus	.....	+	..	Hypophyseal region	6 years	38 years	Pains in eyes	Erosion of posterior clinoid process	Bitemporal hemianopsia and destruction of sella
Dandy.....	1928	2½	F	Plexus	.....	..	+	Sylvian fossa of each side	Since birth	Since birth	Large head	Yes, but not from angioma	.....
Dandy.....	1928	5 mo.	M	Plexus	.....	..	+	Sylvian fossa	1 mo.	4 mo.	Convulsions	None	Convulsions; later in face

X-ray examinations have not been helpful in my cases, for calcified lesions were not present in any of them; nor has any case from the literature been diagnosed from the roentgenograms. In one case, the convolutional atrophy of hydrocephalus was excellently demonstrated, but the large head and Macewen's sign (of separated sutures) had made the evidence given by the roentgenogram unnecessary.

Ventriculography was indispensable in making a diagnosis in two of my cerebellar cases, and ventricular estimation was useful in clinching the localization in another. These methods should always be used when the slightest doubt is entertained either of the existence of a tumor or of the location of a tumor that is known to exist.

*Treatment of Cavernous Angioma.*—Just as is true of angiomatous cysts, or for that matter any kind of tumor, the only satisfactory treat-

was 1½ years old. In thirty patients, the age of onset of the symptoms could be computed. In eleven or about one-third, symptoms began before the tenth year; in eighteen, or 60 per cent, before the twentieth year, and in twenty-five, or 83 per cent, before the age of 30. (Only 16 per cent of the angiomaticous cysts showed symptoms before the thirtieth year.)

The duration of the symptoms shows a contrast almost as striking. Six patients had symptoms for less than one year (three of these died of cerebral hemorrhage and one of operation); four had symptoms for two years; five for three years; and five, for from five to ten years; seven, for from ten to twenty years, and four, for from twenty to thirty years. In the group of patients with angiomaticous cysts, 50 per cent had symptoms less than one year, whereas 80 per cent of those with cavernous angiomas had symptoms longer than one year, and 50 per cent had symptoms longer than five years.

By far the most common symptom of cavernous angioma is epilepsy, and usually the attacks are jacksonian. This is largely due to the fact that most of the tumors are in the cerebral hemispheres and near the rolandic area. It is highly improbable that a cavernous angioma located solely in the cerebellum will cause epilepsy. Many of the patients have had motor or sensory weakness, some slight, some transiently after an attack and others of severe grade.

Headache, vomiting and choked disk are infrequent in cerebral cavernous angiomas because the tumor rarely attains sufficient size to cause intracranial pressure. Rupture of a vessel in the tumor may at once induce intracranial pressure. One of my patients (case 24), with an angioma of the occipital lobe and a big cerebral hemorrhage, had a bilateral papilledema of high grade. Lewandowsky and Stadelmann reported a case presumably of angioma, in which a big cerebral hemorrhage was encountered by a puncture. The patient recovered.

Cavernous angiomas in the cerebellum and brain stem may cause hydrocephalus by closing the aqueduct of Sylvius or fourth ventricle, intracranial pressure then following. A high grade of hydrocephalus was present in all four of my cases of cerebellar cavernous angiomas. In one of these cases, the angioma was small and caused intermittent or recurring hydrocephalus, the tumor acting in ball-valve fashion. It is interesting that over a period of ten years the patient's attacks were intensified in three successive pregnancies. Finally, as the tumor grew, the ball-valve action was largely overcome, for her symptoms rarely abated. In another patient (case 20), slight trauma—presumably causing hemorrhage in the tumor, on several occasions, precipitated paralyzes and general intracranial pressure. The first instance of this relationship occurred when the patient was 14 months old. The early age also indicates the probably congenital origin of the tumor. The relationship of

TABLE 2.—Analysis of Symptoms in Cases

Author	Date of Publication	Age	Sex	Type of Angioma		Tumor		Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
				Cavernous	Small Solid Tumor with Cyst	Single	Multiple						
Baum.....	1911	21	M	..	+ cyst contained yellow fluid	..	..	Left parietal	.....	.....	Convulsions and coma	Coma	Jackson's attack
Bielschowsky..	1903	24	F	..	+ small solid tumor in large cyst	+	..	Right frontal lobe	14 mo.	23 yr.	Headache and dizziness	Choked disk, vomiting, headache	Facial weakness, positive Romberg, increased reflexes
Bruns.....	1897	24	M	..	+	..	..	Left parietal	.....	.....	Convulsions	No	Jackson's attack
Friedrich and Stiebler	1922	41	M	..	+	..	+	Cerebellum	2 yr.	30 yr.	Pain in neck	Headache, vomiting, loss of vision	.....
Koch.....	1913	47	M	+ one side	+ other side	..	+	Each cerebellar lobe	3 yr.	41 yr.	Glycosuria	+	.....
Lindau.....	1926	26	F	..	+	+	..	Cerebellum	5 yr.	21 yr.	Headache	Headache, vomiting, choked disk	Staggering, ataxia, nystagmus, loss of ocular reflex
Lindau.....	1926	50	M	..	+	+	..	Cerebellum	6 mo.	49 yr.	Headache	Headache, vomiting, choked disk	Staggering gait and Romberg, nystagmus
Lindau.....	1926	42	F	..	+	+	..	Cerebellum	4 yr.	35 yr.	Headache	.....	.....
Lindau.....	1920	37	M	..	+	..	..	Cerebellum	5 yr.	29 yr.	Headache	Headache, vomiting, choked disk	Staggering to right, nystagmus
Lindau.....	1926	28	F	..	+	+	..	Cerebellum	1 yr.	27 yr.	Headache and stiff neck	Headache, vomiting	None
Lindau.....	1926	40	M	..	+	+	..	Cerebellum	6 mo.	45 yr.	Headache	Headache, choked disk	Romberg, fall to right
Lindau.....	1926	40	F	..	+	+	..	Cerebellum	1 yr.	30 yr.	Dizziness and staggering	Headache, lumbar puncture	Romberg and staggering
Lindau.....	1926	33	F	..	+	+	..	Cerebellum	2 yr.	31 yr.	Weakness	Headache, vomiting, choked disk	.....
Lindau.....	1926	..	..	..	+	+	..	Cerebellum	.....	.....	.....	.....	.....
Lindau.....	1926	52	M	..	+	+	..	Cerebellum	.....	.....	.....	.....	Loss of left arm and right leg function
Lindau.....	1926	33	M	..	+	+	..	Cerebellum	.....	.....	.....	Choked disk	.....
Lindau.....	1923	32	M	..	+	+	+	Cerebellum and medulla	.....	.....	.....	.....	.....
Lindau.....	1926	38	F	..	+	+	..	Cerebellum	.....	.....	Headache	Choked disk	.....
Luzzatto.....	1925	..	..	..	+	+	..	Medulla	.....	.....	.....	.....	Loss of left arm and right leg function

ment is extirpation, when this is possible. Some tumors lend themselves readily to removal; others present difficulties which are insuperable. One of my patients, a baby 1 month of age (case 21), died of shock when a bloody suboccipital angioma (the continuation of an intracranial tumor) was removed. Bleeding had to be controlled by plugging the big venous spaces in the bone with wax. A second patient, a boy, aged 16 (case 20), died one month after removal of a large cerebellar angioma which had grown into the brain stem. Death was not due to the tumor's removal which he survived, but to closure of the fourth ventricle caused by the formation of a cicatrix between the raw surfaces of the cerebellar

*Cases of Plexiforme Angioma of the Brain*

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
0	0	0	Pain in cheek and teeth	Diplopia	Normal	Tumor ex- posed, but inoperable	Operation	0	Patient was morphine addict; tumor was made up of coils of veins and resembled the well known venous plexus angiomas of the dorsal surface of the cord; the entire tumor could not be seen, nor could necropsy be obtained	0
0	+	0	Cannot sit up but uses both arms and legs	Failure to develop men- tally and to coordinate muscular movements	Imbecile	+ Third ventriculo- tomy for hydrocephalus; angioma disclosed in sylvian fissure	Operation	+	Bilateral plexus of veins (angioma) in each sylvian fissure; several other small plexuses over both hemispheres; absence of corpus callosum; the angiomas did not cause the mental or physical disturbances, they were merely incidental conditions; stricture at iter caused hydrocephalus	0
+	+	+	None	None	Infant	Exploration	Operation	+	Two typical venous plexuses about 2 cm. apart; they were connected by communicating branches and emptied into the sylvian vein	+

lobes and pons from which the tumor had been removed. In this case, the foramina of Luschka had long been sealed by the tumor.

A third patient died before operation. This should have been much the easiest tumor of the group to have extirpated, had it been found at operation. There was a huge blood-filled cavity in the parieto-occipital lobes. The walls of the cavity were rough, having been carved out of the white matter of the brain which hung in shreds in the cavity; in this respect, it was entirely unlike the smooth cyst associated with an intracystic angioma.

Two of the cavernous angiomas were entirely removed, and the patients are apparently well. In one patient (case 22), the tumor was excised from the left lobe of the cerebellum with a margin of cerebellar tissue. It is now over two years since the operation. She is entirely well and without residual cerebellar symptoms.

The other successful extirpation was a tumor laying on the pons and medulla (case 23). During the dissection, the tumor was thought to be a "venous aneurysm," because there seemed to be a single sac with several large venous outlets and because it was so compressible. After

TABLE 2.—Analysis of Symptoms in Cases—

Author	Date of Publication	Age	Sex	Type of Angioma		Tumor		Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
				Cavernous	Small Solid Tumor with Cyst	Single	Multiple						
Newmark.....	....	32	F	..	+	+	..	Cerebellum	1½ yr.	30 yr.	Pain in back of head	Headache, vomiting, choked disk	Occliptal pain, buzzing left ear
Schlafler.....	1926	40	M	..	+	+	..	Cerebellum	9 mo.	30 yr.	Headache	Headache, choked disk	Staggering gait, falls backward to left
Schweyer.....	1914	23	M	+	+	+	..	Frontoparietal lobe	13 yr.	12 yr.	Convulsions	No	Jacksonian attack
Dandy.....	1928	32	F	..	+	+	..	Vermis of cerebellum	7 mo.	31 yr.	Headache	Headache, vomiting, choked disk with positive tremendous retinal hemorrhages	Staggering gait and positive Romberg
Dandy.....	1928	33	F	..	+	+	..	Cerebellum	6 mo.	35 yr.	Headache	Headache, vomiting, choked disk	Staggering gait, Romberg, ataxia, nystagmus, oculokinesis
Dandy.....	1928	44	F	..	+	+	..	Cerebellum Vermis	2 mo.	41 yr.	Dizziness and headache	Headache, vomiting, choked disk	Staggering gait, ataxia
Dandy.....	1928	28	M	..	+	+	..	Cerebellum, left lobe	6 mo.	27 yr.	Headache (in attacks)	Coma, choked disk	Staggering gait
Dandy.....	1928	35	M	..	+	+	..	Cerebellum, left lobe	3 mo.	35 yr.	Occliptal headache	Headache, vomiting, choked disk	Staggering gait, Romberg, ataxia
Dandy.....	1928	34	M	..	+	+	..	Vermis of cerebellum	2 yr.	32 yr.	Pain in eyes and occiput	Headache, vomiting, choked disk	Nervous
Dandy.....	1928	40	M	..	+	..	..	Left cerebellar lobe	1 yr.	30 yr.	.....	Headache, vomiting, choked disk	Staggering gait, Romberg, ataxia

removal and section of the tumor, it was seen to be a typical solid cavernous angioma. The mass was dissected with great care after ligating the large venous outlets as shown in the accompanying drawings (figs. 27, 28, 29 and 30). No artery of size was seen to enter the tumor. There was no injury to the brain stem or cerebellum during the dissection. The patient also is well, one year after operation.

*-Cyst with Angioma in the Wall*

Focal	Epilepsy		Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Ne-eropsy	Remarks	Studied Microscopically
	Petit Mal	Grand Mal								
+	..	+	.....	No	Good	+ with finger extirpation	.....	+	Patient in coma when operated on; no previous symptoms; solid tumor size of walnut; died one year later of pneumonia	+
0	..	0	Dizziness; diplopia	.....	.....	0	Intracranial pressure	+	Large cyst with hazelnut sized solid tumor; cerebellar tumor suspected	+
+	..	+	Weakness in right leg also paresthesia	.....	.....	+	Meningitis, postoperative	+	.....	+
..	..	..	.....	.....	.....	0	Intracranial pressure	+	Small angioma in cerebellum, another in pons and one in medulla	+
..	..	..	.....	Diabetes	Normal	0	.....	+	Patient had von Hippel's disease; cysts of pancreas (with diabetes); cysts and angiomas of liver	+
0	..	0	Left facial paralysis	.....	Normal	0	Intracranial pressure	..	Cyst with angioma—hydrocephalus; cysts of pancreas, cysts of kidneys; hypernephroma	+
0	..	0	Weakness left arm and leg; trigeminal pain	Babinski + loss of corneal reflex	Normal	Decompression	Intracranial pressure	+	Cyst 3 by 2 by 1.5 cm.; tumor 1 by 2 by 1 cm. in upper part of cyst; hydrocephalus	+
0	..	0	.....	.....	.....	0	Intracranial pressure	+	Cyst 5 by 6 by 2 cm.; smooth wall; tumor 1 by 1 cm.	+
0	..	0	.....	Loss of corneal reflex	.....	0	Died 24 hours after spinal injection of air	+	Cyst 6 by 4 by 2 cm.; tumor 1.5 by 1.5 by 0.7 cm.; adenoma of both suprarenal glands; hydrocephalus	+
0	..	0	.....	Both corneal reflexes diminished	.....	0	Intracranial pressure	+	Cyst 3 by 2 by 2 cm.; tumor 1 by 1 cm.	+
+	+	+	.....	Rigid neck	.....	0	Intracranial pressure	+	Cyst 4 by 5 by 2 cm.; tumor 1 by 0.5 cm.; hydrocephalus	+
..	..	..	.....	Adiadokinesia	.....	0	Intracranial pressure	+	Cyst with angioma; hydrocephalus	+
..	..	..	Weakness both legs	Blindness	.....	0	Tonic convulsions	+	Small angioma in cyst.....	+
..	..	..	.....	.....	.....	.....	.....	+	Museum preparation .....	+
..	..	..	.....	Nystagmus blindness	.....	Trephine	Intracranial pressure	+	Cyst 4 by 4 by 1.5 cm.; tumor 1 by 0.5 cm.	+
..	..	..	.....	.....	.....	.....	Intracranial pressure	+	Cyst with angioma in the wall	+
..	..	..	.....	.....	.....	.....	Intracranial pressure	+	Large cyst with angioma; also several small angiomas in cerebellar lobes (largest size of pea) one in medulla	+
..	..	..	.....	Tremor of fingers of both hands	.....	.....	Intracranial pressure	+	.....	+
0	..	0	Weakness of left face	.....	Suggestive of a neurosis	0	.....	+	Patient had a cavernoma of medulla with cyst formation like a syringomyelia	+



TABLE 3.—Cases of Multiple Cavernoma.

Author	Date of Publication	Age	Sex	Type of Angioma		Tumor		Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
				Cavernous	Small Solid Tumor with Cyst	Single	Multiple						
Creita.....	1903	21	F	+	..	..	+	See under remarks	19 yr.	2 yr.	Convulsions	No	No
Finkelnburg...	1905	14	M	+	..	..	+ two	See under remarks	2½ yr.	11 yr.	.....	Choked disk	Staggering gait, left abdominal palsy
Huebschmann.	1921	39	M	+	..	..	+ about 30 in all	Scattered	.....	.....	Convulsions	.....	.....
Jakob.....	1924	34	F	+	..	..	+	See under remarks	20 yr.	10 yr.	Convulsions	Pains in head	Weakness left side; Jacksonian attacks
Kallscher.....	1897	1½	..	+	..	..	+	See under remarks	1 yr.	6 mo.	Convulsions	No	Jacksonian attacks; later paralysis
Kufs.....	1928	51	M	+	..	..	+	Both hemispheres	No symptoms	.....	None	None	None
Malamud.....	1925	51	F	+	..	..	+	See remarks	22 yr.	39 yr.	Headache	Diplopia, headache, dizziness	Symptoms like paralysis after 3 years before death
.....	1923	17	M	+	..	..	+	Caudate nuclei (both sides)	5 days	17 yr.	Headache	Pain in head, coma, bradycardia	.....
Ohlmacher.....	1899	..	..	..	..	..	+	See under remarks	.....	.....	.....	.....	.....
Cases of Cavernous Angioma:													
Astvazaturow	1911	35	F	+	..	+	..	Right frontoparietal	2 yr.	33 yr.	Headache	+	Attacks of face, arm and leg
Astvazaturow	1911	23	F	+	..	+	..	Right temporal lobe	12 yr.	10 yr.	Convulsions	No	Jacksonian epilepsy
Bail.....	....	10	M	+	..	+	..	Left Rolandic area	2 yr.	8 yr.	Convulsions	+ choked disk	Jacksonian epilepsy
Bremer, d'Antona	Ref. Lechner	20	M	+	..	+	..	Parietal	.....	.....	Convulsions	.....	Jacksonian attacks; later paralysis of the right arm
Bremer and Carson	Ref. Lechner	23	..	..	..	..	..	Subcortical	.....	.....	.....	.....	.....
Cassirer and Muhsam	1911	22	M	+	..	+	..	Right parietal post-central	5 yr.	17 yr.	Convulsions	Headaches since youth	Jacksonian attacks; later paralysis of the right arm

## REPORT OF CASES OF CAVERNOUS ANGIOMA

CASE 20.—*Cavernous Angioma of the Cerebellum and Brain Stem.*

The patient was a very well nourished boy, aged 16, with a large head. He had been bedfast for sometime and sought relief for headache, disturbance of

*Cyst with Angioma in the Wall—Continued*

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Ne-eropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
0	+	0	.....	Attacks of moment's loss of consciousness	Normal	0	Intracranial pressure	+	Pea sized tumor in extracerebellar; collection of yellow fluid (left cerebellar lobe)	+
..	..	..	Bilateral Babinski	Dizziness	.....	Extirpation with lobe of cerebellum	Living	..	Large part of cerebellum removed with tumor	+
+	..	+	None	None	Normal	0	Status epilepticus	+	Cyst size of cherry, filled with blood; tumor size of small walnut alongside; some calcification	+
0	0	0	Occasional attacks of numbness of right arm and leg	Stiff neck dizzy attacks	Normal	Removal	Living and well, 5 years	..	In a large cyst filling the vermis was a small papilloma (angioma); it lay over the midbrain; totally removed; vision has returned to normal	+
Tonic spasms of whole body; no loss of consciousness			Transient ankle clonus on right	Dizziness; stiffness of neck; diplopia	Normal	Removal of angioma in the wall	Living, 2 mo.	..	A half pea-sized angioma was located in the tonsil of cerebellum	+
Tonic spasms but no loss of consciousness			Positive Babinski	Dizziness	Mental cloudiness	.....	Intracranial pressure	+	Cyst in vermis of cerebellum tiny plaque of angioma over region of the midbrain	+
0	0	0	Reflexes normal	Dizziness diplopia	Normal	Removal of angioma	Living; 7 years since operation	..	Localization of tumor by ventriculography	+
0	0	0	Reflexes normal	Blind; dizziness; stiff neck	Normal	Removal of angioma	Living; 4 years	..	Ventricular estimation test substantiated cerebellar localization	+
0	0	0	Numbness and tingling in right arm and leg	.....	Normal	Removal of angioma	Living; 6 months	..	Localization of tumor made solely by ventriculography	+
..	..	..	.....	.....	Normal	.....	Intracranial pressure	+	Patient died before reaching hospital	+

vision, disturbance of gait and projectile vomiting. His symptoms dated back to the age of 14 months, when he had fallen a distance of 4 feet, striking the back of the head on a brick. He had been unconscious for only a few minutes, but immediately afterward had become paralyzed on both sides. The father, who is a physician, insisted that both sides were paralyzed at that time. After three weeks, the paralysis had gradually cleared up; both sides had improved about the same time. The father said further that the child had been talking for about

TABLE 3.—Cases of Multiple Cavernous Angiomas:  
Cases of Cavernous

Author	Date of Publication	Age	Sex	Type of Angioma		Tumor	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
				Cavernous	Small Solid Tumor with Cyst	Single						
Levick.....	1914	9	F	+	..	+	.. Cerebellum	Rapid progression	.....	Paralysis	Headache	Cerebellar symptoms
Lindau....	1926	48	M	+	..	+	.. Cerebellum	6 yr.	42 yr.	Headache	Vomiting, headache, choked disk	.....
Lindau....	1926	..	..	+	..	..	.. Cerebellum and pons	.....	.....	.....	.....	.....
Dandy.....	1928	16	M	+	..	+	.. Vermis of cerebellum	15 yr.	1 yr.	Paralysis bilateral after slight trauma	Large head, choked disk, convolitional atrophy of skull, headache, vomiting	Hydrocephalus; staggering gait; Romberg
Dandy.....	1928	1 mo.	M	+	..	+	.. Suboccipital intra and extra-cranial	Before birth	Tumor was present at birth	Tumor	Hydrocephalus with large head	Tumor resembles meningocele
Dandy.....	1928	35	F	+	..	+	.. Left cerebellar lobe	10 yr.	25 yr.	Headache	Headache, choked disk	Partial paralysis on left
Cases of Cavernous Angioma in												
Berblinger....	1922	27	M	+	..	+	.. Medulla	13 yr.	14 yr.	Paralysis	+	Paralysis first one arm, then other
Enders.....	1908	60	M	+	..	+	.. Left side of pons	.....	.....	Convulsions	No	Attack began in right side of body
Leyser.....	1922	20	F	+	..	+	.. Pons 1 by 3 mm.	20 days	20 yr.	Coma	Coma	.....
Nalim.....	1928	11	M	+	..	+	.. Fourth ventricle	9 mo.	10 yr.	Headache	Coma (no choked disk)	Staggering gait, ataxia, nystagmus, Babinski
Nambu.....	1907	63	..	+	..	+	.. Pons	.....	.....	.....	.....	.....
Selmbach.....	1927	28	F	+	..	..	.. Fourth ventricle	5 yr.	23 yr.	Headaches	Headache, loss of vision	Staggering gait, ataxia, nystagmus, Babinski
Tophoff.....	1925	28	F	+	..	+	.. Pons	.....	.....	.....	.....	.....
Wohlwill.....	1927	28	F	+	..	..	.. Fourth ventricle spinal cord	5 yr.	23 yr.	+	+	Weakness in legs
				with von Hippel's								
Dandy.....	1928	31	M	+	..	+	.. On pons and medulla	2½ yr.	20 yr.	Stiffness of right leg in spells	Headache, choked disk, diplopia, loss of vision	Numbness, tingling, weakness in legs

# Angioma of the Brain from the Literature

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Ne-cropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
0	..	+	No	.....	.....	0	Convulsions	+	Eight isolated tumors—all of same small structure; six are scattered through both cerebral hemispheres, another is in the cerebellum and one in the pons; vessels greatly calcified	+
0	..	0	.....	Diplopia, difficulty in urination, pains in back and limbs	.....	0	Pressure	+	Small tumor in corpora quadrigemina; larger one in fourth ventricle and extends into spinal cord; tumor causes hydrocephalus	+
..	..	+	.....	.....	.....	0	Convulsions	+	About thirty tiny angiomas were scattered throughout brain	+
+	..	+	Weakness left side	Intention tremor, ataxia, dysarthria	.....	0	Convulsions	+	Three tumors were present—all small: (1) in fundibulum, (2) in pons, (3) in fourth ventricle	+
+	..	+	Weakness right side	.....	.....	0	Convulsions	+	Left hemisphere studded with small tumors on all surfaces; hemiplegia gradually developed	+
0	..	0	None	.....	Sense dementia	0	Sensility	+	Nevl in skin presumably related; daughter had apoplexy (recovery) at age of 17; dozen small tumors scattered throughout white matter of brain, one in posterior horn, another in pons; multiple cavernomas in liver	+
0	..	0	.....	Extra-ocular palsies, queer feeling in both hands	Attacks of euphoria, depression and apathy	0	.....	+	Tumors (1) in region of infundibulum and third ventricle (1.5 by 2.75 cm.); (2) in right pallidum (3 by 5 mm.); (3) in pons, and medulla (4) several others scattered in left hemisphere	+
..	..	..	.....	Extra-ocular palsies, cervical rigidity	.....	.....	Hemorrhage	+	Small tumor in caudate nucleus of each side; patient died five days after first symptoms of hemorrhage	+
..	..	..	.....	.....	.....	0	.....	+	Three angiomas were present—all small; (1) colossal gyrus; (2) optic thalamus; (3) spinal cord; an osteoma and a fibroendothelioma were also present	+

## Fronto-Parietal Region of the Brain

+	..	+	.....	Loss of memory	Retrograde amnesia	0	Meningitis	+	Tumor size of "mark"; vessels thrombosed and calcified	+
+	..	+	.....	Loss of memory	Loss of memory	0	Convulsions	+	Tumor extends deeply into hippocampus	+
+	..	+	.....	.....	.....	0	Convulsions	Large tortuous mass of tumor veins on surface	Attacks followed two weeks after slight head injury; possibly an arteriovenous aneurysm	-
+	..	+	.....	.....	.....	+	.....	..	.....	-
..	..	+	.....	.....	.....	+	.....	..	Tumor size of a nut.....	+
+	+	-	Loss of touch eventually	Weakness of hand after attacks	Slow at school	÷ removed	Living	..	Patient complained of headache after exertion; no difficulty with hemorrhage when tumor excised	-

three months prior to the injury, and that after the blow on the head speech had been lost but had returned with the motor function. His head had always been large, but the father explained that this was a family characteristic; all of the father's brothers had large heads. The boy, however, wore a 7¾ hat, while the size of his father's hat was 7½; his grandfather wore a No. 8. During the convalescence from the injury to the head, the patient had vomited a great deal and had cried much after the initial drowsy period wore off. Even after six weeks, the vomiting and crying had persisted. The patient had continued to have headaches and spells of vomiting up to the age of 6 years; at this time he had been thrown from a horse and had been unconscious for about half an hour. During the next two days, he had been unable to stand. He had always been more clumsy than the other children, and his movements were slower and less sure. After the age of 6, the clumsiness had increased. When he was 2½ years old, it had been noticed that a crossed eye had developed without warning; the right eye drew in toward the nose. For sometime after the injury to the head (at the age of 6), the eyeball had not moved; this condition had improved gradually during the next six months, some weakness of the external rectus muscle persisting. Until the age of 12, there had been little change in his condition. He could not read well because of the extra-ocular palsies; his clumsiness seemed to increase, and he became weaker and had a tendency to deviate to the right side while walking.

At the age of 12, he had tripped and fallen on the right side of the head while running at school. He had been unconscious for twenty minutes and drowsy for several days; during this time he had had a fever and his temperature had been as high as 103 F.; he had complained of a severe headache. Again he had been unable to walk for a period of sixty-one days, and during all of this time he had complained of severe headaches. After two months he had begun to walk, but only with support. Two weeks later, he had been able to stand alone. For the following two years, nothing unusual had happened, and then without warning the headaches had reappeared and had occurred more or less constantly; they were always severe and occurred every two or three weeks.

A year before operation, the boy's father had noticed that his disturbance of gait, awkwardness and clumsiness were still persisting. At this time, it had been noticed that he staggered definitely toward the right. Two months before operation, the patient had become progressively worse, and during all of this time he had been confined to bed.

Examination showed a rather sallow, fat boy with a large bony frame and poor musculature. He complained of severe headache. His large head was disproportionate to the development of his body, and showed a marked cracked pot sound on tapping along the frontoparietal sutures. The veins of the eyelids and scalp were prominent and full. The eyegrounds showed a slight choking of both disks, perhaps a little more marked on the right; the temporal margins, however, were still visible. Weakness of both external rectus muscles produced an evident strabismus. There was slight but definite weakness of the right facial muscles. His hearing was impaired on both sides, but air conduction was better than bone conduction. The entire right side of the body was definitely weaker than the left. There was a marked positive Romberg sign, and he always fell to the right. Ataxia was present in both hands, but more on the right. There was adiodokinesis on both sides, more on the right, and nystagmus in both directions. Reflexes were equal and active. The Babinski sign was absent. X-ray examination showed separation of the suture.

*of the Brain from the Literature—Continued*  
*Angioma in Cerebellum*

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Men- tality	Opera- tion	Cause of Death	Ne- cropsy	Remarks	Studied Micro- scopically
Focal	Petit Mal	Grand Mal								
0	..	0	Weakness of left leg and face	Occipital pain, re- flexes in- creased on left	.....	Removal +	.....	No	.....	+
..	..	..	.....	.....	.....	.....	Intraeranal pressure	+	Large solid angioma in cere- bellar lobe, mostly capillary spaces, others larger	+
..	..	..	.....	.....	.....	.....	.....	+	Three angiomas, one in pons and two in cerebellum; all very small—museum specimen	+
0	0	0	Bilateral at times	Strabismus	Normal	+ Removal of tumor	Hydroceph- alus	+	This angioma had grown into the medulla and pons; on several occasions slight trauma induced signs and symptoms suggestive of hem- orrhage into the tumor	+
0	0	0	None	None	Baby	Removal of extra- cranial tumor	Shock	+	Very large tumor outside the skull and another even larger inside and directly beneath; both were continuous by ex- tension of tumor directly through occipital bone	+
0	0	0	Numbness of left side after spell of headache	Anosmia	Normal	Removal	Living and well	..	Tumor was removed with zone of normal cerebellar tissue; complete recovery; localiza- tion made by ventriculog- raphy	+

*Brain Stem and Fourth Ventricle*

0	..	0	Paralysis	Urinary incontinence	Normal	0	.....	..	Associated with von Hippel's disease	+
+	..	+	No	.....	.....	0	Convulsions	+	Tiny tumor in pons, more to left side	+
0	..	0	Paralysis	.....	.....	0	Hemorrhage (?)	+	.....	+
0	..	0	.....	.....	.....	0	Intracranial pressure	+	Tumor filled fourth ventricle, pushed into pons; hydro- cephalus	+
..	..	..	.....	.....	.....	.....	.....	+	Small tumor .....	+
0	..	0	Left-sided paralysis	Difficulty in urination	.....	0	Intracranial pressure	+	(1) tumor size of walnut in fourth ventricle; (2) another in dorsal spinal cord; (3) retinal angioma (von Hip- pel's disease); (4) cysts of pancreas and kidney	+
..	..	..	.....	.....	.....	0	Apoplexy	+	Patient died of apoplexy.....	+
+	..	+	Weakness left side of body	.....	.....	0	Intracranial pressure	+	Tumor size of hazelnut in roof of fourth ventricle; another tumor (2 cm.) in dorsal cord; von Hippel's tumor of retina; cysts of pancreas and kidney	+
0	0	0	Numbness and weak- ness of left side, increased at times	Loss of vision, uncertain gait, but not stag- gering	Normal	Removal	Living and well	..	Tumor completely removed (by dissection) from floor of fourth ventricle	+

resection with the tumor. Preparatory to this section, the veins on the surface were ligated, and the large veins which ran from the surface of the cerebellum to the tentorium were doubly ligated and divided. The incision was then carried through the cerebellar cortex beyond the confines of the tumor (fig. 20). Much to my surprise, no vessels of moment were encountered during this part of the dissection. The hemispheres were retracted to either side. The tumor then remained attached only to the floor of the fourth ventricle, i. e., the pons and medulla.

The anterior surface of the mass was found to be well defined and ended just posterior to the aqueduct of Sylvius. The portion of the fourth ventricle between the aqueduct and the obstruction was greatly dilated, and the aqueduct was as large as one's little finger. The release of this fluid greatly facilitated the operation. The dissection was then begun along the floor of the fourth ventricle. There was no line of cleavage; the mass of fibrous tissue was densely adherent to the brain stem, and from this source the large veins were seen to enter, as at the previous operation. There seemed to be no alternative than to deliberately cut through



Fig. 21 (case 20).—Operative attack on the tumor over the medulla and pons. This was the only difficult part of the extirpation.

the mass just above the floor of the ventricle, and to control the bleeding with silver clips and with packs. It now seemed fairly certain that the lesion was not an arteriovenous aneurysm and that the struggle with hemorrhages would be mainly with veins. Much to my surprise, however, these enormous veins bled relatively little, and many of them were thrombosed; it was possible to cut through the entire scar with little bleeding, and this was readily controlled (fig. 21). The mass of tumor was then lifted out of its bed. The wound was closed without drainage.

Recovery from the immediate effects of the operation was uneventful. The patient did not have any immediate effects from the removal of the tumor mass. He lived one month after the operation. About ten days after the operation, it was evident that the hydrocephalus still persisted, for there was steadily increasing pressure on the cerebellar wound.

Necropsy showed that the three sides of the raw surface produced by the extirpation of the tumor had closed together and had again completely closed the fourth ventricle. All of the vascular fibrous mass had been removed, except the portion which was deliberately left on the floor of the ventricle.

It was evident that the patient had a cerebellar lesion and presumably a tumor. It was also evident that this lesion had been present since the age of 14 months, so that it must have been congenital. As the symptoms of localization and those of general pressure increased after slight trauma, it seemed probable that the lesion must have been a tumor which was readily susceptible to hemorrhage. The diagnosis of a cerebellar tumor was made.

*Operation.*—On June 19, 1925, a bilateral cerebellar exposure was made. The lesion was at once evident in the vermis and the mesial side of both cerebellar lobes; it presented a brownish discoloration and was extremely hard and inelastic. Although sharply circumscribed, it was not encapsulated. In order to gain a better impression of the lesion, the foramen of Magendie and the fourth ventricle were exposed. The cerebellar lobes were separated in order to reach the tumor in the fourth ventricle. After proceeding about 2 cm. along the floor of the fourth ventricle, several large veins were encountered running directly out of the brain stem into the hard indurated mass of tumor, which was continuous with the mass described on the surface. The entire fourth ventricle was obliterated at its level



Fig. 20 (case 20).—Drawing to show position and character of the cavernous angioma. The gross character of this tumor borders on that of a plexiform angioma. The dotted line indicates the line of incision for resection of the tumor laterally. Since there was no plane of cleavage between the tumor and the brain stem, the tumor was sectioned directly above the medulla and pons, leaving a fragment of the angioma attached thereto. Many of the vessels were thrombosed and as all of the bleeding was venous the excision of the tumor was not accompanied by much hemorrhage despite its vascular construction. The tumor had completely closed the fourth ventricle and produced hydrocephalus.

by the tumor, which did not give any outward evidence of being more than dense fibrous tissue. As large veins were present everywhere and were coming directly out of the medulla, extirpation seemed hopeless. The wound was closed.

The patient's condition remained practically unchanged for the next ten days. After further thought and in view of the hopeless nature of the lesion, I was persuaded to make an attempt to remove the tumor, though it was clear that it would be necessary to carve the tumor from the brain stem, into which it had grown.

*Second Operation.*—On June 30, 1925, the cerebellar wound was reopened. The entire vermis and the inner margin of each cerebellar lobe was then prepared for



*Operation.*—At operation, the lesion was quickly recognized as a tumor. It was intimately attached to the skull and was so bloody that at every attempt to separate it from the skull applications of wax were necessary to stop bleeding. The pericranium was everywhere absent, the bone rough and irregular from the extensive adherence of the tumor and the many vascular channels which penetrated it. Nowhere was an opening seen to penetrate the bone. For this reason, it was evident that the tumor was not causing the hydrocephalus. It was equally evident that another tumor, presumably of the same angiomatic type, must be present in the posterior cranial fossa, and causing the hydrocephalus. Necropsy proved this assumption to be correct. An equally large tumor was present in the posterior

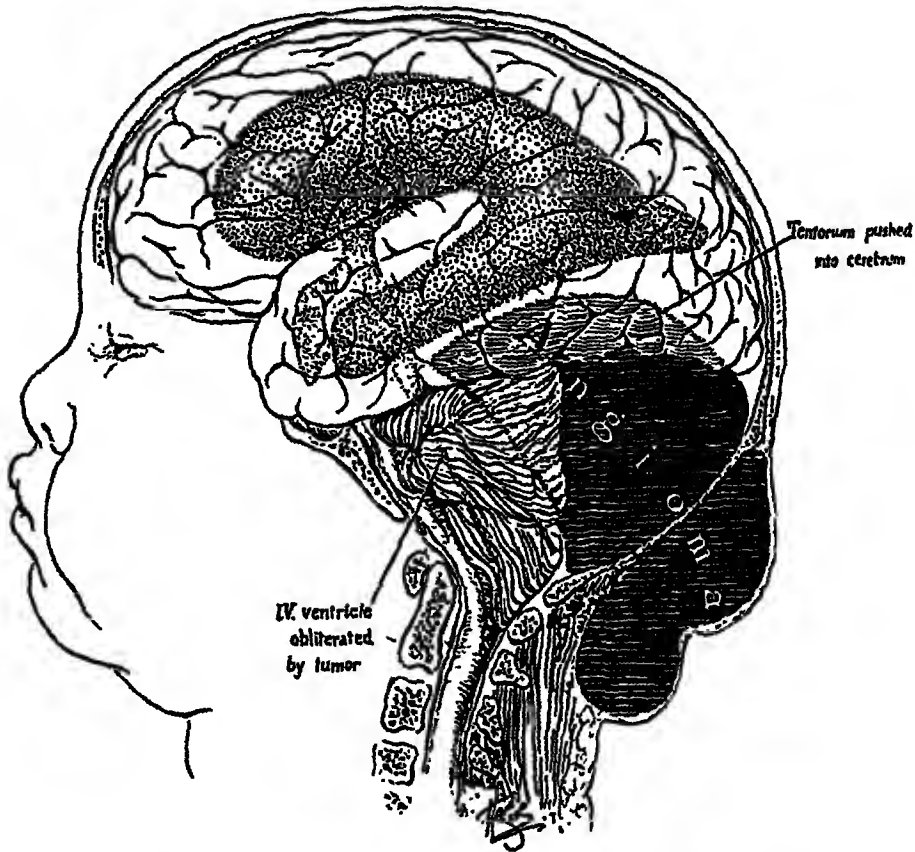


Fig. 23 (case 21).—The position and relative size of the tremendous angioma shown in figure 22. The tumor pushed the cerebellum far forward thereby causing the tentorium to bulge. It has completely occluded the fourth ventricle causing a hydrocephalus of high grade.

cranial fossa. It was attached to the inner surface of the occipital bone, and lay immediately beneath the external tumor. The internal and external tumors were directly continuous through the bone by angiomatic extensions of microscopic size.

Both intracranial and extracranial tumors were alike; they were soft, sponge-like and compressible. Blood could be expressed from the spaces which were of varying size up to nearly 1 cm. in diameter.

The microscopic appearance showed the tumor to be a cavernous hemangioma.

The microscopic diagnosis was cavernous angioma. It doubtless was of congenital origin.

**CASE 21.—Cavernous Angioma in Posterior Cranial Fossa and Extracranial Suboccipital Region.**

An infant, aged 1 month, was referred by Dr. W. P. McDowell, of Norfolk, Va., because of a lump in the back of the head, presumably an occipital meningocele (figs. 22 and 23). The tumor had been present since birth and was then about double the size at birth. The whole head had also been rapidly increasing in size during the three weeks before operation. Before this time, the head had not



Fig. 22 (case 21).—Photograph of patient with a large extracranial and intracranial cavernous angioma. The position of the tumor suggested an occipital meningocele.

seemed unusually large. Convulsions had not occurred, neither had there been nausea or vomiting. The swelling was exactly in the midline in the suboccipital region; it was of oval-shape and measured about 5 by 5 by 7 cm. It was everywhere covered by normal skin, and did not show any evidence of nervous tissue. It was compressible and seemed to pulsate. At the time of operation, the diagnosis of meningocele was made, though doubtless had the light transmission test been made it would have changed this diagnosis. X-ray examination would also have excluded a meningocele, for there was no opening in the center of the occipital bone. Advanced obstructive hydrocephalus was diagnosed by ventricular estimation.

It is noteworthy that except for a subjective cervical rigidity and the possible disturbance of hearing, there were no indications of a cerebellar lesion. The loss of smell and the possible uncinata attacks suggested a lesion in the uncinata gyrus (temporal lobe).

Ventriculography showed a bilateral hydrocephalus with a large third ventricle (figs. 24 and 25).

*Operation.*—On Dec. 29, 1925, cerebellar exploration was performed. A tumor appeared in the left cerebellar lobe. It reached the surface beneath the lateral sinus, to which it was attached by filmy adhesions. Two tortuous veins passed over the cerebellum and entered the tumor. A large artery also passed into the tumor from below. A third vein skirted the tumor. After the vessels on the surface of the cerebellar lobe had been tied, the tumor was removed by resecting



Fig. 25 (case 22).—Anteroposterior ventriculogram of the same patient. The symmetrical, dilated lateral ventricle and the mesially placed third ventricle (also enlarged) indicate the position of the tumor to be in the posterior cranial fossa.

a good margin of cerebellar tissue around it (figs. 26 and 27). The subcortical part of the tumor was not seen at any time until the resected mass was sectioned for study. The tumor was then seen to be composed entirely of a meshwork of blood-containing spaces with some interposed connective tissue. A diagnosis of cavernous angioma was made.

The postoperative course was uneventful. The patient did not suffer any noticeable ill effects of the loss of the cerebellar tissue. She has remained well to date, over two years after operation.

#### CASE 23.—*Cavernous Angioma of the Fourth Ventricle.*

A healthy looking man, aged 31, was referred by Dr. Samuel Key of Austin, Tex. Two years before admission to the hospital, his right leg had occasionally

**CASE 22.—Cavernous Angioma of Left Cerebellar Lobe.**

A well nourished woman, aged 35, was referred by Dr. Walter B. Martin, of Norfolk, Va., with the diagnosis of an unlocalized tumor of the brain. Her symptoms had begun ten years before when during a pregnancy she had had severe headaches in the frontal and temporal regions of both sides. The headache had shifted slowly to the back of the head. Since this time, she had had headaches of the same character about every six months; each attack lasted about from six to eight weeks. The headaches began gradually, increased steadily, reaching a maximum usually in about six weeks. She was then forced to stay in bed. They then disappeared gradually. The disappearance of the headaches could not be accounted for any more than their beginning. Nausea and vomiting accompanied

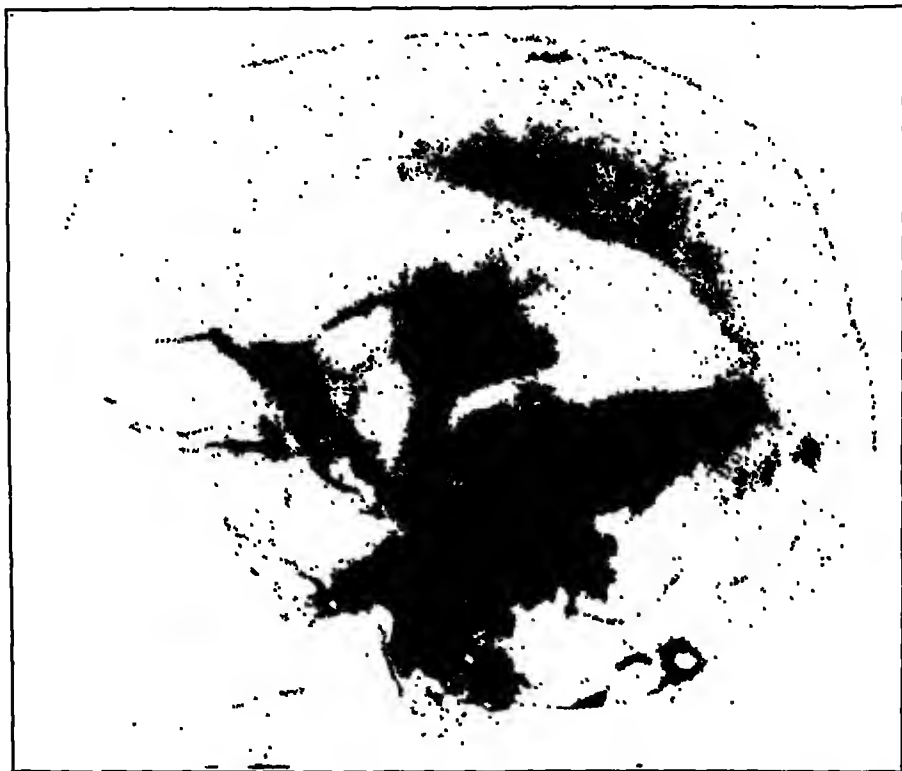


Fig. 24 (case 22).—Lateral ventriculogram. This patient had signs and symptoms of intracranial pressure, but none of the tumor's location. The ventriculogram shows greatly enlarged lateral and third ventricles.

the headaches. During one of these attacks of headache, she had partially lost the hearing in the left ear. Eight months before operation, in one of these spells, she had lost the sense of smell and taste, and since then had constantly smelled a nauseating odor of "burnt celluloid." Her last attack of headache had begun about twelve weeks before operation and persisted until that time. In this attack she felt some numbness in the left arm and leg and stiffness in the neck. There was no diplopia.

Neurologic examination showed the following positive conditions: (1) double choked disk, about equal on the two sides; (2) complete loss of smell; (3) 50 per cent loss of hearing—bone and air conduction in left ear.

dragged and become stiff. For seven or eight months, there had been some weakness in the fingers of the left hand. The fingers on the right hand had also become numb and stiff, but less than those on the left hand.

Six months before operation he had begun to have attacks of blurred vision: since this time, he had had several such attacks daily. Dimness of vision would last half an hour or more after each seizure. Later his vision had been greatly limited "on both sides." He had never had headache, but in the morning when getting up there had frequently been pain back of the right ear. When he held his neck stiff, this pain seemed to disappear.

About four months before operation, he had suddenly fallen to the floor unconscious. When he awakened, he was in bed but felt well. He did not bite his tongue and was not incontinent. Three weeks before operation, he had had a similar attack. He did not know whether he had had a convulsion.

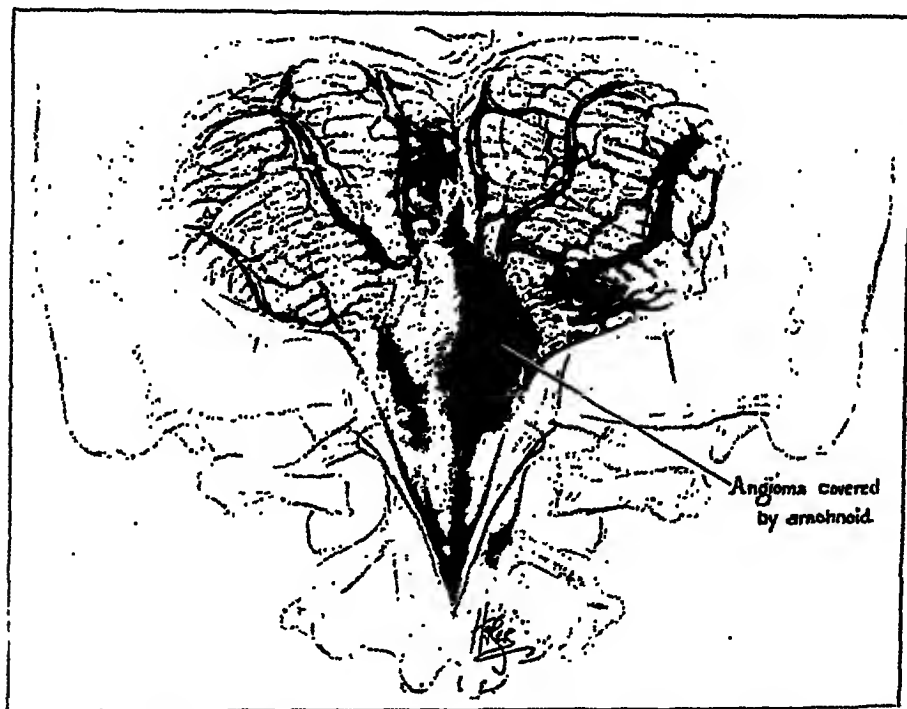


Fig. 28 (case 23).—Bulging tumor between the cerebellar lobes and over the medulla. It is covered with arachnoid which must be split before the tumor can be exposed.

The positive neurologic observations were: (1) bilateral choked disk (4 diopters in each eye); (2) visual fields greatly reduced; visual acuity 20/100 in each eye; (3) definite motor loss in left arm and leg; (4) definite hypo-esthesia in left arm and leg; (5) uncertain gait, but not staggering (Romberg sign negative); (6) slight nystagmus in right lateral fixation. It is noteworthy that all of the reflexes were normal. The x-ray picture showed destruction of the posterior clinoid processes.

Ventriculography showed high grade bilateral hydrocephalus with large third ventricle (figs. 31 and 32).

*Operation.*—On July 28, 1927, bilateral cerebellar operation was performed. A strictly midline tumor was found between the cerebellar lobes and resting directly on the medulla and pons (fig. 28). When first seen, it was covered with arachnoid

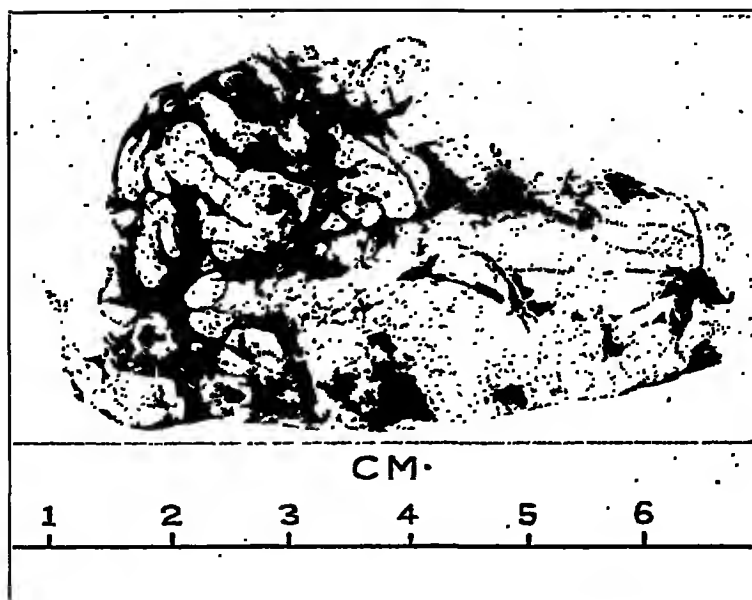


Fig. 26 (case 22).—Cavernous angioma removed with an area of cerebellar tissue surrounding it. The tumor has just reached the surface of the cerebellum at a point near the middle of the resected mass.

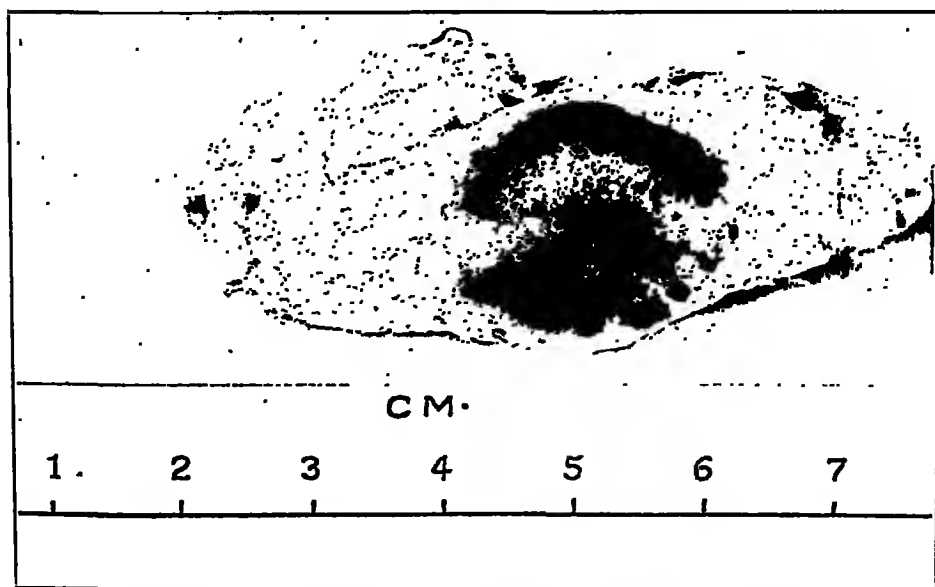


Fig. 27 (case 22).—Cross-section of resected cerebellar tissue and the tumor shown in figure 26.

After two weeks in bed, he had felt well enough to be up and about, but for five months he had felt groggy and tired. He had then returned to work. A month later, when arriving at the office, he had suddenly had an attack of severe vertigo, and two hours later had experienced violent nausea and vomiting, all of which had lasted for twelve hours; objects had seemed to whirl about him. Diplopia had also appeared at that time. There had been a queer feeling in the eyes, and his neck had been stiff. He said that he thought he had staggered at times, but that the dizziness may have accounted for this. He had improved gradually, and eight days later had again left the bed. For the next year and a half, he had done little work and had rested a great deal.

He had again been referred by Dr. Sprunt, in March, 1928, because bilateral choked disks had been discovered. He did not complain of headaches and felt

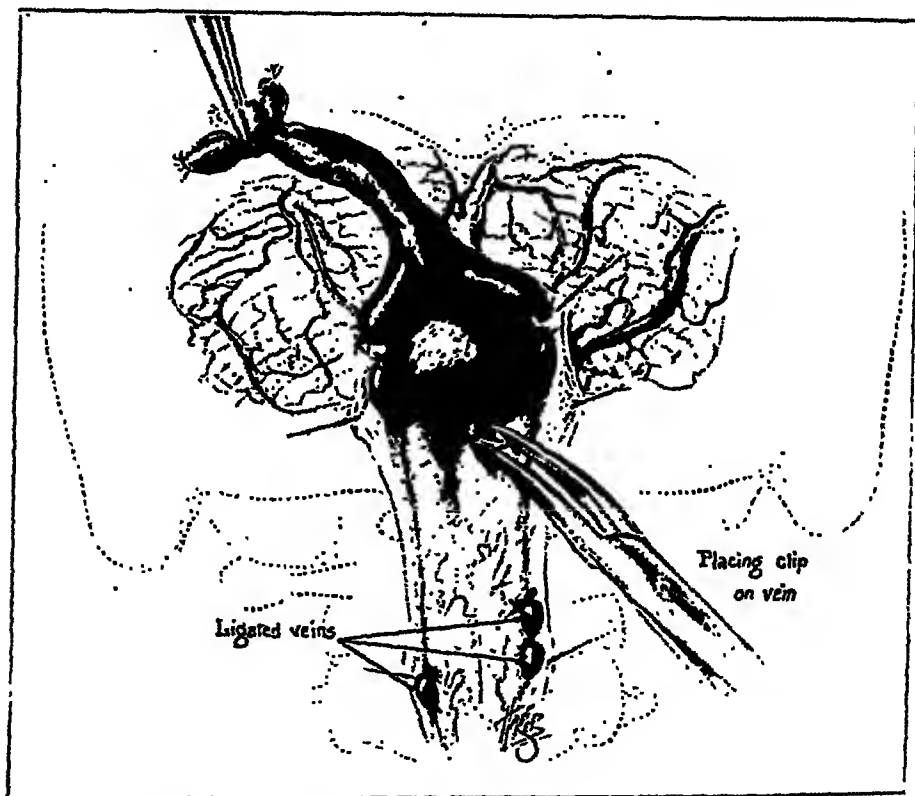


Fig. 30 (case 23).—Operative removal of tumor shown in figures 28 and 29. On elevating the tumor a single large vein passed into the medulla precisely in the midline. This vein was occluded with a silver clip and, after the division of the vein above the clip, the tumor lifted out in its entirety. Throughout the dissection of the tumor no artery of size was seen to enter it. There was practically no bleeding during the removal of the tumor.

that his recovery, though not complete, had been steadily progressive. He said that the dizzy feeling was still present when his head was suddenly turned to the right.

Except for a bilateral papilledema of 4 diopters in each eye, the results of the physical and neurological examinations were negative. It was my impression that the patient had a tumor of the brain, probably a cyst with an intracystic papilloma. The long duration of the symptoms with periods of marked improvement would

and was thought to be a glioma, but after the membranes had been split, it was seen to be a well encapsulated tumor. There was an oval, smooth, bluish, fluctuant central mass closely attached to the brain stem. From this tumor, which had every appearance of a venous aneurysm (it did not pulsate and imparted no thrill), three large veins, larger than slate pencils, emerged (fig. 29). One vein came from the vault of the tumor and passed over the right side of the pons and was lost to view; the second emerged from the vault of the tumor and passed over to the left side of the medulla, and the third passed from the lower pole of the tumor, down the center of the spinal cord and at the level of the axis (the atlas had been removed posteriorly), two branches passed over the right side of the spinal cord and one over the left. All of these veins were carefully ligated, after which the central tumor mass was carefully elevated from its bed in the brain stem (fig. 30). One other vein, slightly smaller than the one already mentioned, emerged from the exact center of the under surface of the tumor and passed directly into the medulla near its junction with the pons (fig. 30).

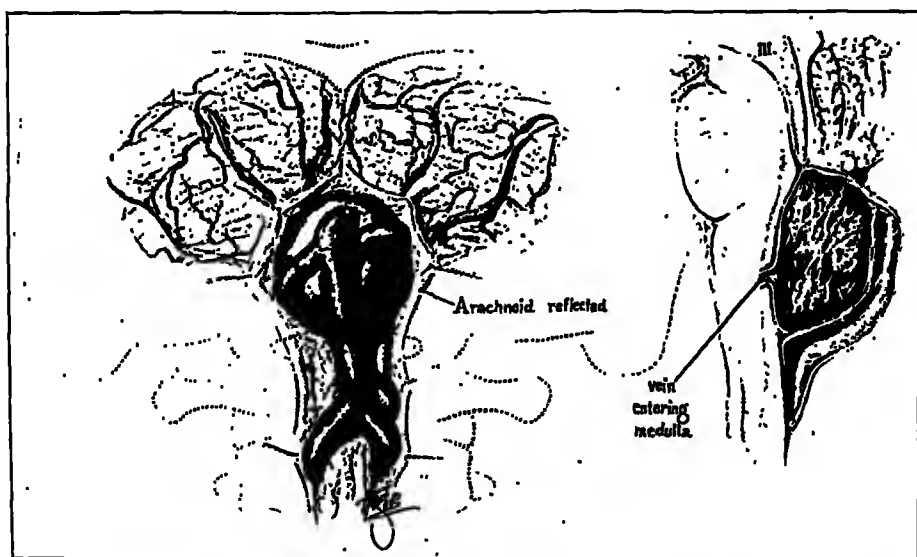


Fig. 29 (case 23).—Tumor exposed after splitting the arachnoid. The large veins issuing from the tumor suggested at first that the tumor was a venous sac (venous aneurysm). The five large veins which emerged from the tumor were ligated with silk; the tumor was then lifted upward and dissected from the brain stem to which it was loosely attached.

The patient promptly recovered from the operation which was without incident, except that there was some increase in the incoordination in the left hand. This disturbance soon improved, and when seen seven months later he was perfectly well except for a very slight weakness—far less than in the left hand on admission.

**CASE 24.—Cavernous Angioma of Occipital Lobe with Hemorrhages.**

A normal looking man, aged 32, was referred by Dr. T. P. Sprunt, of Baltimore, in October, 1926. In February, 1926, the patient had had a spell of severe pain in the legs and arms, more on the left side. The pain had not been constant, but had occurred in waves. He had continued at work for ten days, when persistent nausea and vomiting had developed. He could not retain food.



seem to indicate a cyst. The sudden symptoms on several occasions suggested hemorrhages from the tumor. Because of the rigidity of the neck and the outspoken dizziness,<sup>3</sup> particularly on turning the head to the right, a presumptive localization of the tumor was made in the cerebellum.

An injection of air into the cerebral ventricles was advised for the accurate localization of the tumor, to be followed by the exploration of the tumor in anticipation of its removal if possible.

The patient was scheduled to enter the hospital a week later, on March 17, 1928. Suddenly, on March 16, 1928, he complained of violent dizziness and headache. A few minutes later, he was deeply comatose and had Cheyne-Stokes respirations. He was rushed to the hospital, but became cyanotic and died as he entered the operating room. In an attempt to resuscitate him, a ventricular puncture was performed quickly in first aid fashion. A spurt of dark blood (hemorrhage) followed the right occipital puncture, but his pulse did not beat again and respiration did not commence. It was then clear that he had had a cerebral hemorrhage in the right occipital lobe.

Necropsy showed a large, oval cavity (as large as one's fist) in the right occipital lobe and extending into the temporal lobe (fig. 33). The cyst was about

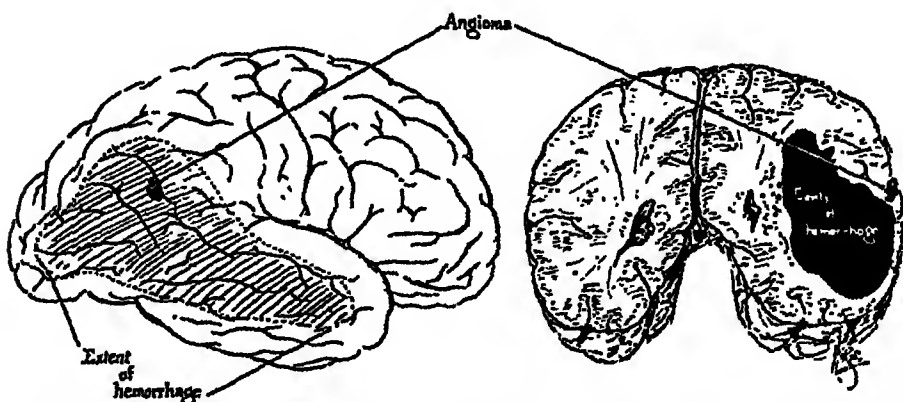


Fig. 33 (case 24).—Sketch of the brain (at necropsy) showing the position and extent of a large hemorrhage and small angioma. This patient died before operation.

from 1 to 2 cm. below the surface of the brain. At first a tumor could not be seen, but on more careful inspection, a small, smooth swelling was noted in the region of the angular gyrus. At first it was thought to be merely the indentation of a convolution, but cross-section demonstrated a small mass of loose, spongy tissue measuring about 1 by 1 cm.; it replaced the cortex and connected with the pia-arachnoid (fig. 34). It was clearly an angioma.

The microscopic diagnosis was cavernous angioma.

*Relationship of Angiomas of the Brain to Angiomas and Other Congenital Lesions Elsewhere in the Body.*—The frequency of multiple angiomas in the brain must prepare one to believe that the same lesions

3. This case was recently reported in a paper dealing with dizziness in Ménière's disease, brain tumors and other lesions, as an example of this type of dizziness associated with tumors located elsewhere than in the posterior cranial fossa. (Arch. Surg. 16:1127 [June] 1928).

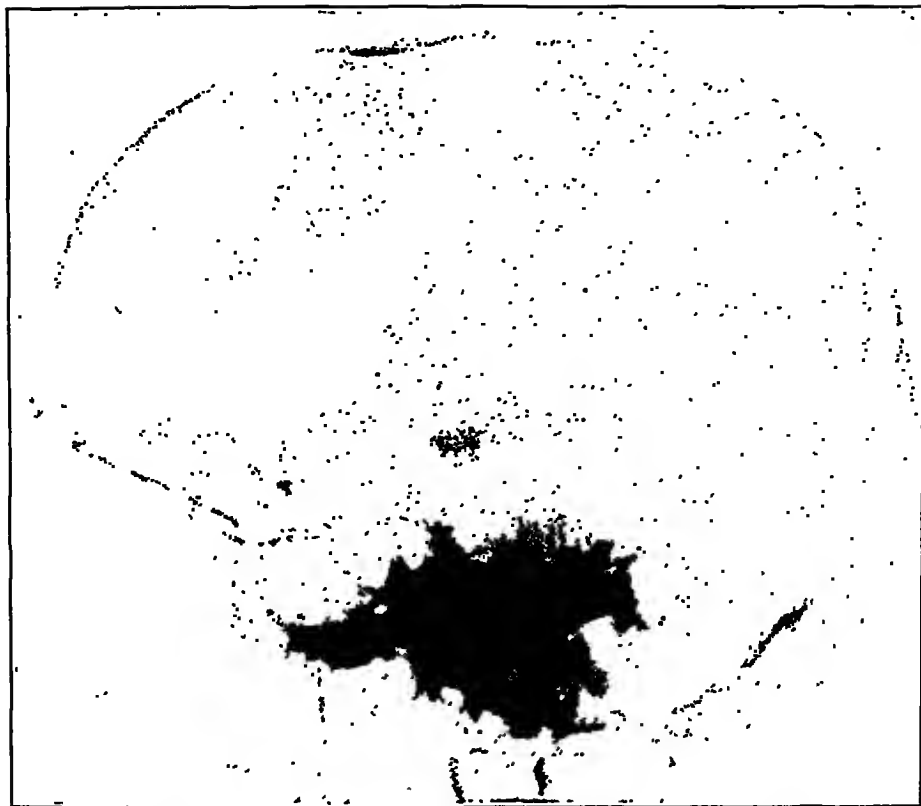


Fig. 31 (case 23).—Ventriculogram of tumor shown in figures 28, 29 and 30. It was situated far enough anteriorly to block the foramina of Luschka and produce a big hydrocephalus. Doubtless the block was of ball-valve character, for the tumor must have been present since birth. The patient is now 31 years old.

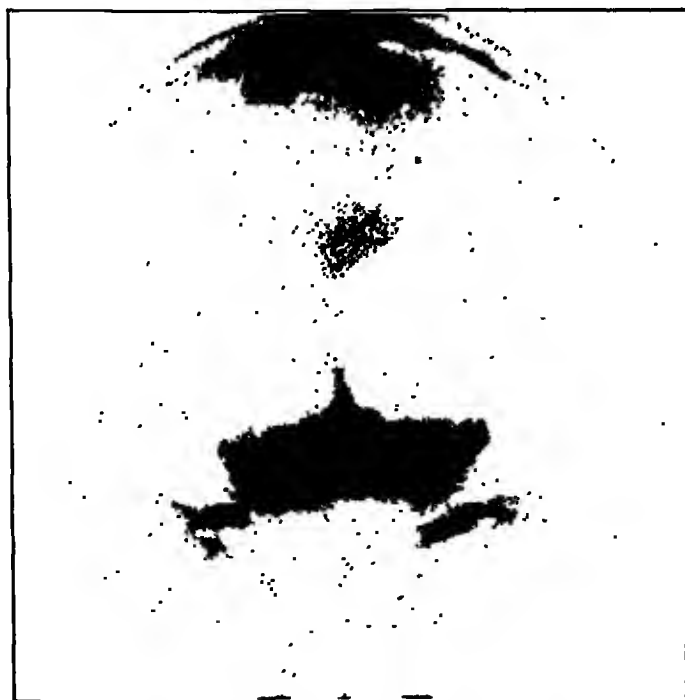


Fig. 32 (case 23).—Same as figure 31.

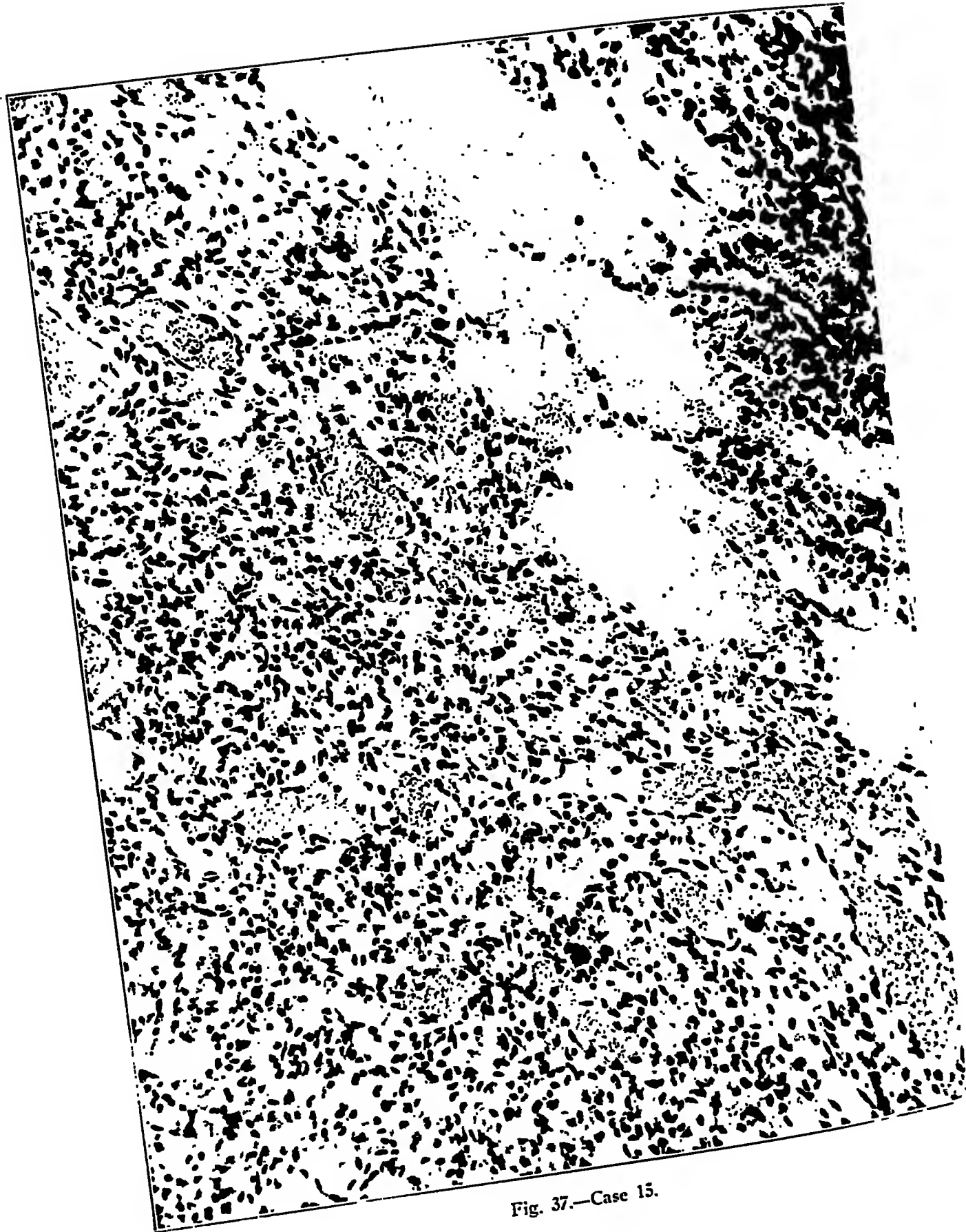


Fig. 37.—Case 15.

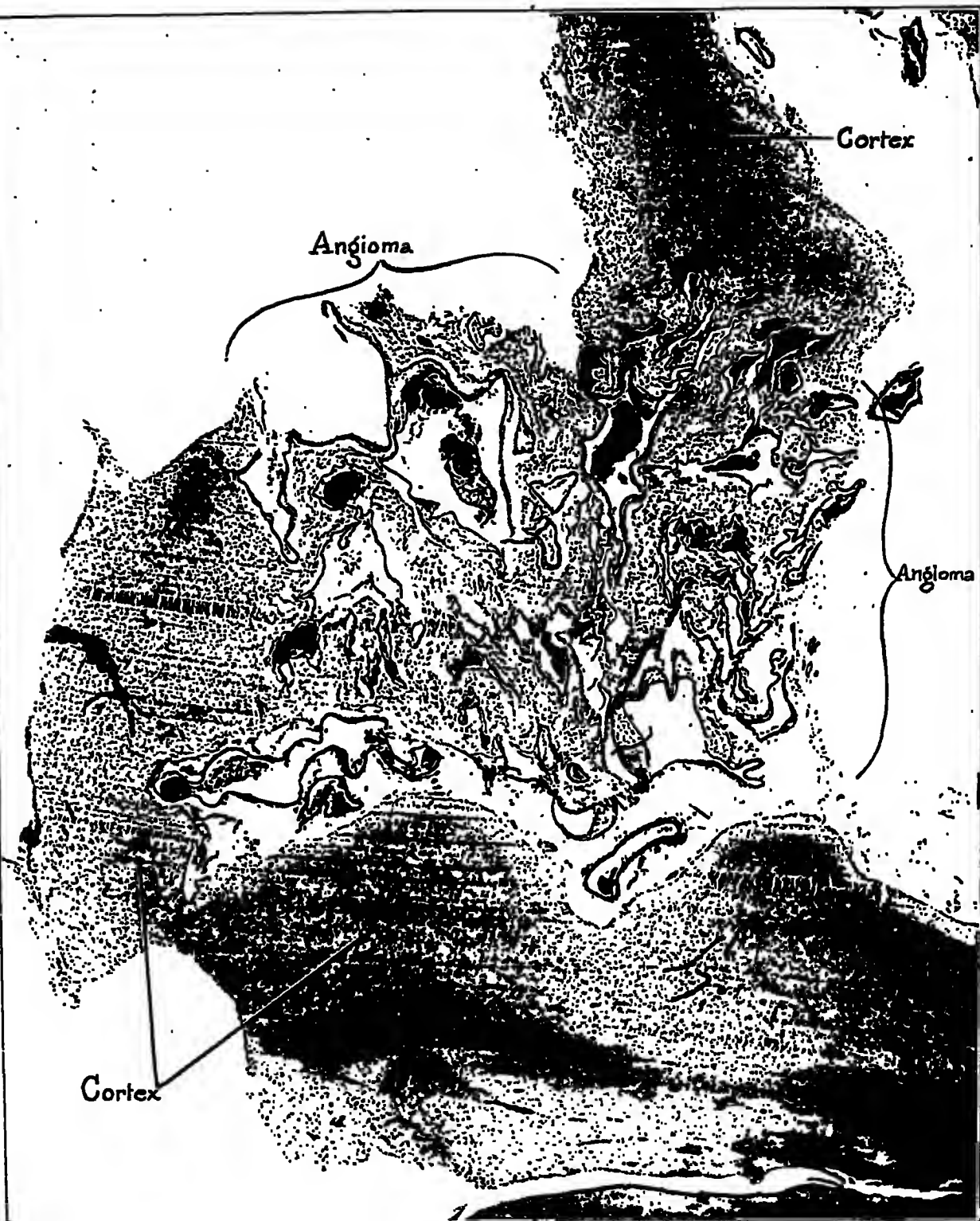


Fig. 34 (case 24).—Photomicrograph (low grade) showing relationship of an angioma to the cortex in an occipital lobe. To remove an angioma of this character it is necessary to include the cortex just beyond its border. This also makes its extirpation much easier because the vascular tumor is avoided. Spontaneous hemorrhage is always a danger, even in a seemingly insignificant and dormant angioma.

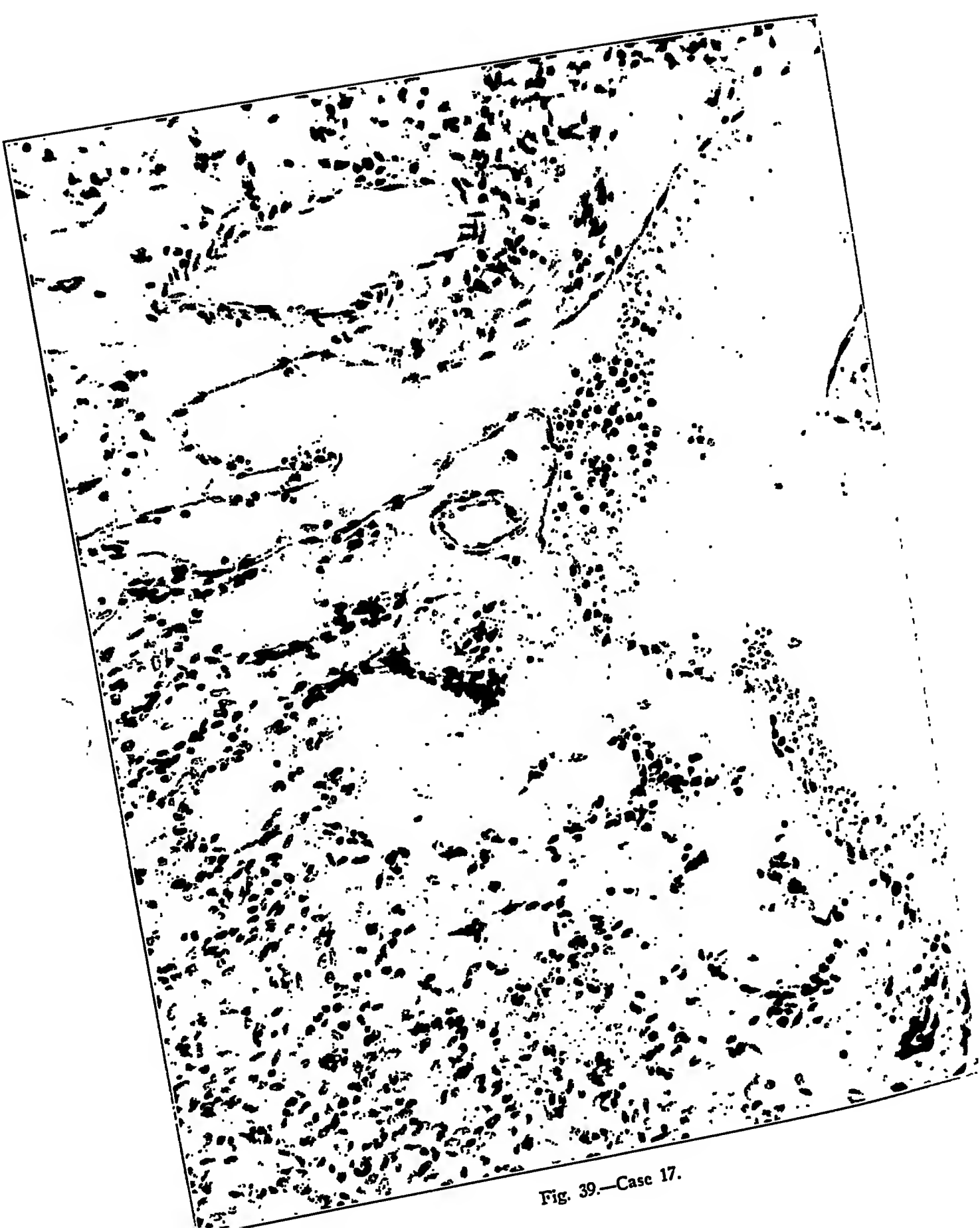


Fig. 39.—Case 17.



Fig. 38.—Case 16.



Case 211 Showing perforation of the bone by the angiomatous spaces.



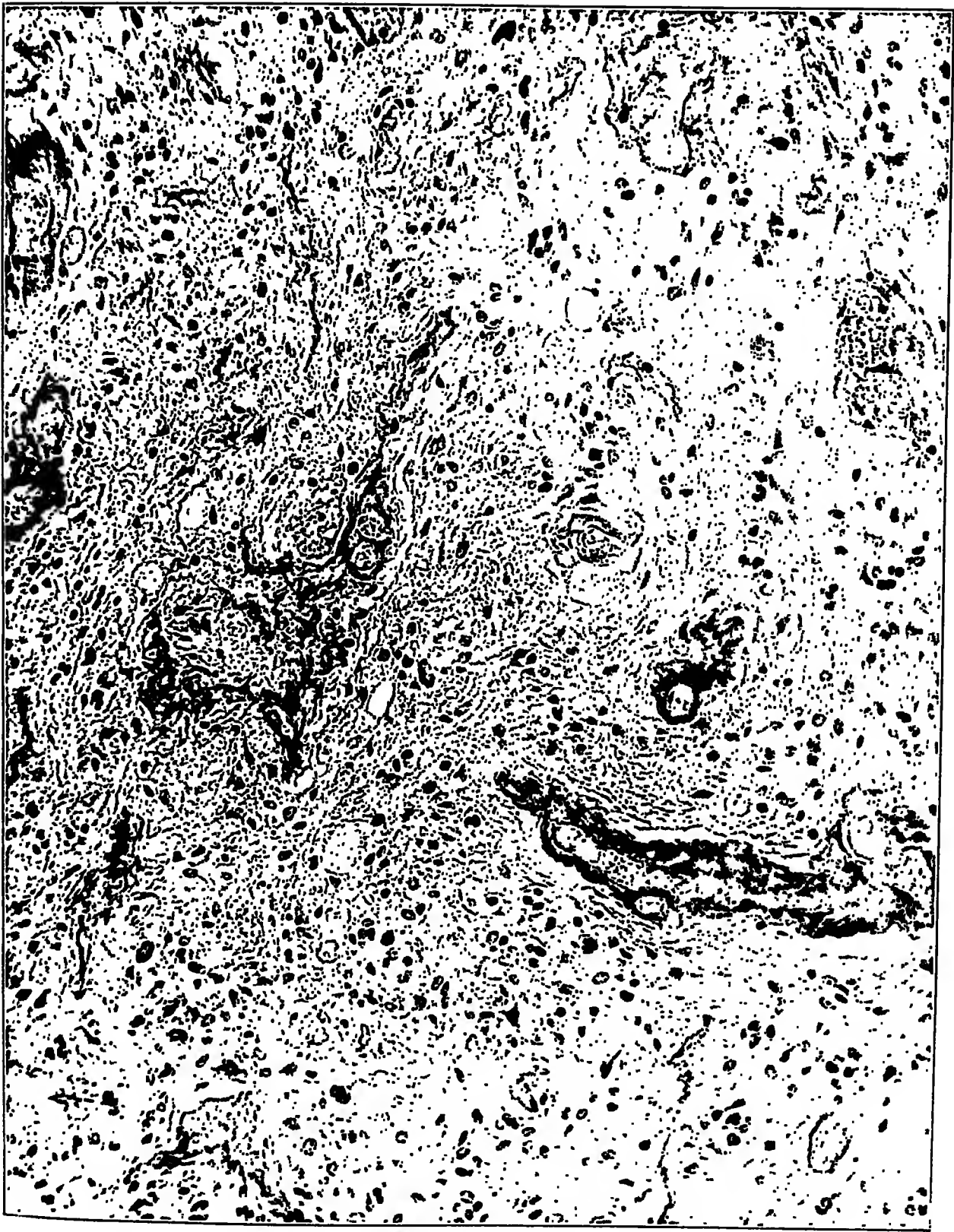


Fig. 40.—Case 18.



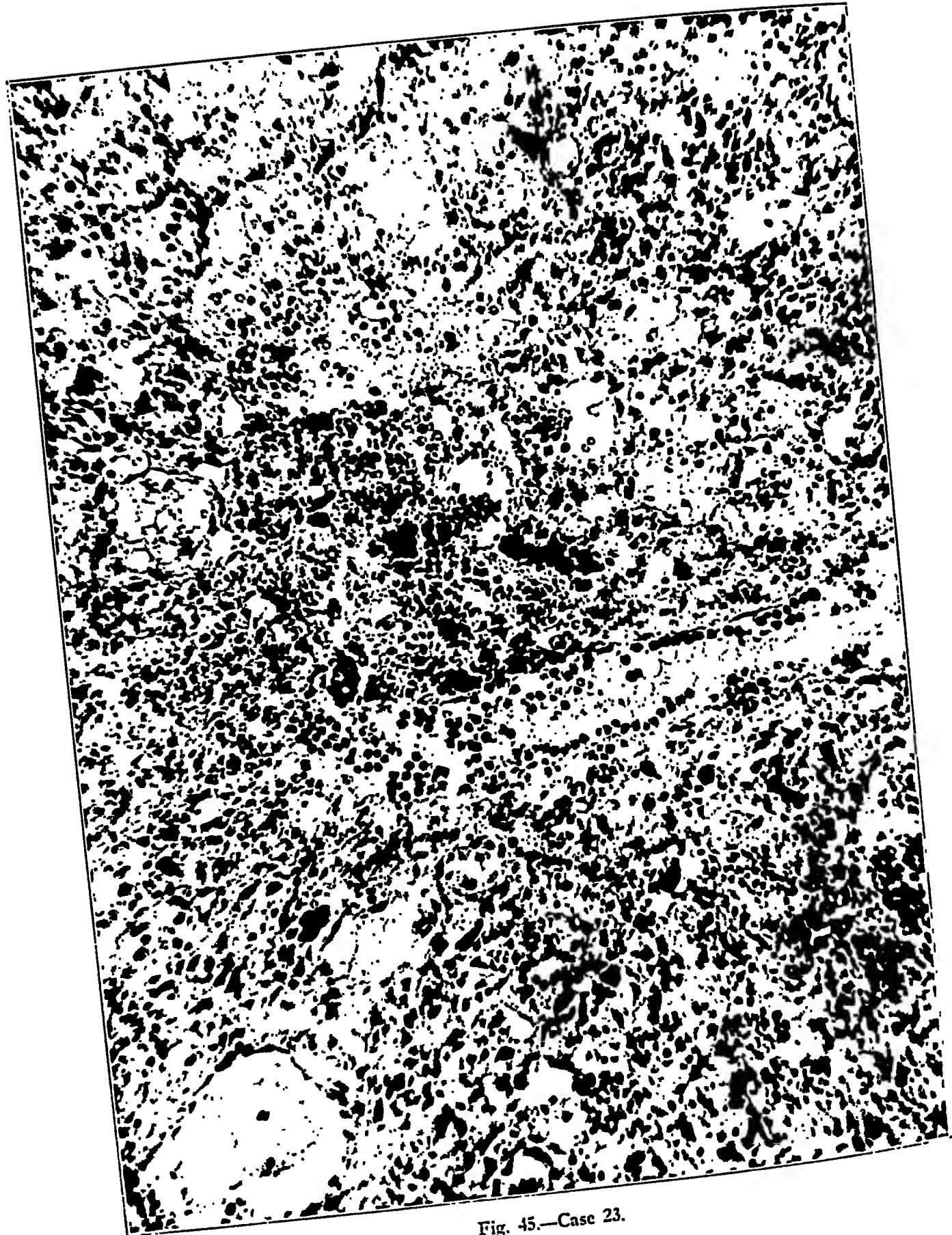


Fig. 45.—Case 23.



Fig. 44.—Case 22.

nothing can be contributed toward a better knowledge of the relationship between angiomas of the brain and cysts of the abdominal organs.

#### SUMMARY AND CONCLUSIONS

1. A series of cases of venous anomalies, plexiform angiomas, angiomatous cysts and cavernous angiomas of the brain are reported. The additional cases of similar types are collected from the literature, and their clinical features are analyzed.

2. The venous anomalies are of congenital origin. Their clinical symptoms are usually epilepsy and disturbances of mentality. They are frequently associated with other deformations of the brain.

3. Three cases of angioma plexiforme are reported. They resemble a similar lesion well known in the spinal cord.

4. A network of venous spaces in the dura and communicating freely with the longitudinal sinus is offered as a cause of focal epilepsy beginning in the leg or arm. Its constant location suggests that it is probably the congenital remains of an embryonic dural circulation.

5. Angiomatous cysts exist throughout the brain, but with greatest frequency in the cerebellum. The size of the tumor embedded in the wall of the cyst is relatively insignificant. Intracranial pressure develops rapidly because of the cyst formation and the resultant hydrocephalus. Localizing symptoms are usually, but not always, present. These tumors cannot be differentiated clinically from other types of cysts of the brain.

6. Cavernous angiomas assume many gross appearances. They are scattered throughout the brain, but appear to occur with greatest frequency in the frontoparietal region. The predominating symptom of this type of tumor is jacksonian epilepsy with or without transient or permanent motor weakness. Pressure symptoms will develop if the tumor is situated near the ventricular channels or outlets. The typical tumors begin early in life; they grow slowly, and the symptoms endure for many years. A clinical diagnosis can be made at times.

7. Hemorrhage from the tumor is always a potential danger in all types of angiomas, though to a less degree than in arteriovenous aneurysms of the brain.

8. Both the cavernous angiomas and the angiomatous cysts should be treated surgically by complete removal of the solid tumor together with a margin of contiguous brain tissue. Both of these types of tumor offer good prospects of complete cure and with relatively little risk. The tumors in the cysts are among the easiest tumors of the brain to extirpate.

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must occur concomitantly elsewhere in the body, especially when it is recognized that these lesions are peculiar to the vascular system and not to the brain. Strominger (1903) demonstrated one of the early cases of cavernous angioma of the brain and called attention to an associated extensive nevus of the face which he considered highly significant. Finkelnburg's (1905) patient had a cyst of the cord in addition to angiomas of the corpora quadrigemina and fourth ventricle. Koch's (1913) patient had diabetes mellitus, and at necropsy, cysts of the pancreas, cavernous angiomas of the liver, an angiomatous cyst of one cerebellar lobe and a cavernous angioma of the other lobe were found. In addition, his patient had von Hippel's disease, i.e., so-called angiomatosis retinae. This was the first instance of the association of the vascular lesion in the retina (assumed to be an angioma) and an angioma of the brain. In 1913, Oppenheim presented to the medical society four patients, in each of whom he suspected an angioma of the brain because congenital nevi of the face and body existed in association with longstanding symptoms of cerebral origin, mainly paralyses and convulsions. Although none of his diagnoses were checked by necropsy or operation, Oppenheim said, "An angioma of the brain must always be considered when vascular naevus of the face are present." Berblinger (1922) reported another case of von Hippel's disease in a patient who had a cavernous angioma of the body.

The association of angiomatosis of the central nervous system with angiomatosis retinae (von Hippel's disease) and cysts of the pancreas, liver and spine attained new importance with Lindau's splendid publication. He thinks that cysts or cavernous angiomas in the cerebellum occur in 20 per cent of all cases of angiomatosis retinae. In half of his cases of angiomatous cysts of the cerebellum, there were cysts of the pancreas; and in two-thirds, cysts of the kidneys. Lindau considered these disturbances of the brain, retina, pancreas and kidneys a congenital maldevelopment complex. Since Lindau's publication, Schuback (1927) and Wohlwill (1927) have published reports of cases of angiomas of the brain in which cysts of the spinal cord, pancreas and kidneys and angiomatosis retinae existed. Kufs (1928) reported a remarkable case of angioma of the brain with nevi of the body and many cavernomas of the liver. This patient's daughter had had a cerebral hemorrhage (from which she had recovered) at the age of 17. Kufs looked on this hemorrhage as a rupture of an angioma, and thought that the family indicated a hereditary basis for the angioma.

In none of my cases has von Hippel's disease been observed, although the eyegrounds have always been carefully examined. The retinal picture is so striking and characteristic that, once seen, it could not be missed. As most of the pathologic material was obtained at operation,

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# LIGATION OF THE TERMINAL ABDOMINAL AORTA

## AN EXPERIMENTAL STUDY \*

BARNEY BROOKS, M.D.

ALFRED BLALOCK, M.D.

AND

G. S. JOHNSON, M.D.

NASHVILLE, TENN.

The greater portion of the experimental investigation which has been conducted heretofore for the study of the effects of occlusion of the abdominal aorta has been concerned with the changes in the volume of flow of blood through the posterior extremities and with the development of a collateral circulation. The fact that death has so often followed obstruction of the abdominal aorta in man has been frequently ascribed to the effect of this procedure on the heart. The purpose of this study was primarily to observe the effects of occlusion of the abdominal aorta on the heart.

The importance of such a study is apparent from the consideration of the different views which have been expressed in two recent reports of successful ligation of the abdominal aorta. Matas<sup>1</sup> described the changes in a patient who lived for approximately one year after almost complete occlusion of the abdominal aorta. It is evident from this report that Matas believes that occlusion of the aorta produces important effects on the heart. He states:

It is really surprising that the myocardium, enfeebled by a protracted and most virulent syphilitic infection, a generalized polyarthritis of the spine, hip and knee-joint, accompanied by a constant high fever for months, should have survived the continued strain of aortic and pulmonary obstruction imposed upon the heart by the total occlusion of the abdominal aorta.

More recently, one of us (B. B.<sup>2</sup>) reported a case in which the abdominal aorta was completely occluded for a period of three months. In discussing the effect of this procedure on the heart, it was stated:

The heart was believed to be slightly enlarged before operation. At the time of death, three months after operation, the heart was found to be essentially normal. There was, therefore, no indication in this instance of the occlusion of the abdominal aorta affecting the heart in any way.

A similar difference of opinion has been expressed by two previous investigators who have studied this problem by experimental methods.

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\* From the Department of Surgery, Vanderbilt University Medical School.

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The following possible objections to the experimental method require discussion: (1) the influence of the anesthetic and (2) the influence of the operative procedure necessary for the occlusion of the aorta. In regard to the anesthetics used, the possible influence of morphine on the cardiac output was controlled by the studies on the trained animals in which anesthetic was not used. In these experiments, the cardiac output was determined without any anesthetic. The animal was then given an anesthetic and the aorta occluded. The cardiac output was subsequently determined after recovery without any anesthetic. As regards the effect of ether anesthesia, in other experimental work not included in this paper, one of us (A. B.) has shown that the administration of ether in an amount comparable to that used in these experiments always results in an increase in the cardiac output. An example of an experiment showing the influence of ether on the cardiac output is given in table 1. It has already been adequately established that neither of the

TABLE 1.—*Effect of Ether Without Operation on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O <sub>2</sub> Consumption, Cc. per Minute	<i>p<sub>H</sub></i>	Cardiac Output, Cc. per Minute	Output per Kg., per Minute, Cc.	Output, per Beat, Cc.
5/12/26 Control study, $\frac{3}{4}$ grain morphine .....	8.6	70	99	15.35	8.85	6.48	17.1	90	73.95	7.35	1141	132.7	16.3
5/12/26 After ether for 7 minutes .....	8.6	150	99	14.04	11.04	3	17.22	82	59.04	7.29	1908	223.0	13.1
5/12/26 After additional ether. ....	8.6	150	99	14.40	11.40	3	.....	..	58.4	7.30	1947	226.4	13.0
5/12/26 2 hours after stopping ether .....	8.6	76	98.5	15.24	8.06	6.58	.....	..	75.64	7.36	1148	133.4	15.1

Protocol: 5/12/26, control study performed after giving  $\frac{3}{4}$  grain of morphine. Dog then given ether anesthesia through a mask seven minutes until the eye reflexes were barely abolished, and a determination of the output made. The ether was discontinued for a few minutes and then the animal was again given an anesthetic for seven minutes and another determination of the output made. The last studies were made two hours after the ether was discontinued. Animal was quiet during all the observations.

drugs used as an anesthetic in the amounts used in these experiments causes any appreciable alteration in blood pressure. The possible influence of the operative procedure necessary for ligation of the aorta was controlled by determinations of the cardiac output and blood pressure in five experiments in which the abdomen was opened and the aorta isolated without being occluded. This procedure was usually followed by a definite increase in the cardiac output and produced only temporary changes in the blood pressure. The results of these experiments are shown in tables 2 and 3.

## RESULTS

It is obvious that it is impossible to make observations on both the blood pressure and the cardiac output on a single animal for more than a relatively short period of time by the methods used in this study. In most of the experiments, therefore, the effects of occlusion of the aorta on the blood pressure and on the cardiac output were

Kast,<sup>3</sup> from a series of experiments in which he studied the effect of obstruction of the aorta on the blood pressure, found that there was little, if any, change in the blood pressure in the artery proximal to the site of occlusion. From these experiments, Kast concludes that ligation of the abdominal aorta is not to be considered as endangering life from its effect on the heart. Katzenstein,<sup>4</sup> from a similar experimental study, found that occlusion of the abdominal aorta resulted in an elevation of the blood pressure in the artery proximal to the site of obstruction, and that animals having had the abdominal aorta obstructed for a considerable period of time showed dilatation and hypertrophy of the heart. From these experiments, Katzenstein concludes that obstruction of the aorta results in placing on the heart of the patient an extraordinarily great strain.

The basis of this paper is the observations of the effect of occlusion of the abdominal aorta on the blood pressure, the cardiac output and the distribution of the blood volume.

#### METHODS

Dogs were used in all experiments. For the operative procedure necessary for occlusion of the aorta, some form of anesthetic was always employed. Ether was usually given for the opening of the abdomen and isolation of the vessel. All of the observations on blood pressure were made on dogs anesthetized with morphine. Some of the determinations of cardiac output were made on dogs trained to submit to this procedure without anesthetic. The blood pressure was determined by placing cannulas, which were connected with mercury manometers, in the carotid and femoral arteries. The cardiac output was calculated from the determination of the oxygen content of samples of blood from the right and left heart, taken during a period in which the consumption of oxygen was measured. The consumption of oxygen was determined by a Benedict spirometer with the graphic recording device. The animal was connected with the spirometer either by the use of a specially constructed mask which fitted tightly over the mouth or by a tube placed in the trachea. Specimens of blood for gas analyses were withdrawn with the usual precautions from the right and left ventricles. The oxygen and the carbon dioxide of the specimens of arterial and venous blood were determined by the use of the Van Slyke-Neill<sup>5</sup> manometric apparatus. The circulatory minute volume was calculated from the Fick formula:

$$\frac{\text{Cc. O}_2 \text{ consumed per minute}}{\text{Amount of O}_2 \text{ taken up in lungs by 1 cc. of blood}} = \frac{\text{Number of cubic centimeters of blood flowing through lungs per minute.}}{1}$$

In all experiments in which the animals were to be studied for long periods, an aseptic operative technic was employed, and the complete obstruction of the abdominal aorta was made certain by the division of the vessel between ligatures or the careful examination of the vessel at autopsy. In all experiments in which the effect of the occlusion of the aorta on the cardiac output was determined, one or more control determinations of the cardiac output were made previous to the institution of any other experimental procedures.

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4. Katzenstein, M.: *Arch. i. klin. Chir.* 76:581, 1905.

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The rate of the consumption of oxygen usually remained about the same after occlusion of the aorta as in the control period. The decrease in cardiac output was, therefore, manifest for the most part by an increased difference between the oxygen contents of the samples of arterial and venous blood. The arterial oxygen content was found unchanged or slightly higher after the occlusion of the aorta. The arteriovenous difference was usually changed by variation in the oxygen content of the venous blood. There was a slight increase in the oxygen capacity in those experiments in which this was determined. The pulse rate increased in varying degrees.

TABLE 8.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO <sub>2</sub> , per Cent by Volume	Venous CO <sub>2</sub> , per Cent by Volume	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Bent. Cc.
9/30/26												
Control study; no morphine.	8.0	120	102	14.84	9.05	5.19	83.72	37.45	102	1965	222	16
10/2/26												
Control study; no morphine.	9.2	115	102.6	15.08	9.60	5.48	80.94	45.33	113.0	2062	224	18
10/5/26												
Control study; no morphine.	9.0	115	102	15.08	9.41	5.67	80.11	45.74	112.5	1984	220	17
10/6/26												
24 hours postoperative; no morphine .....	8.7	180	102.2	14.84	10.02	4.82	37.31	39.66	94.5	1961	225	11
10/7/26												
2 days postoperative; no morphine .....	8.5	180	103.2	12.77	6.04	5.83	40.06	42.17	90.0	1544	182	9
10/10/26												
No morphine .....	7.7	150	104	9.93	2.91	7.02	35.61	37.42	101	1439	187	9

Protocol: Healthy young male dog. 9/30/26, 10/2/26 and 10/5/26, control studies without morphine. 10/5/26, aorta ligated twice above trifurcation and cut between ligatures, the lowest lumbar artery on the right side was also ligated. 10/6/26, animal able to walk using left foot, but drags the right one. Studies made twenty-four hours after operation without morphine. 10/7/26, twenty-four hours after ligation, determinations without morphine. Animal still unable to use his right leg in walking. The right leg is definitely cooler than the left. 10/10/26, dog does not look well, but is able to walk. Superficial infection of incision. Discharge from nose. Determinations. 10/12/26, animal died. Nothing found at autopsy, to account for death. No pneumonia. No apparent enlargement of heart. No thrombi in heart. Ligature on aorta in place, no thrombosis. No peritonitis. No gangrene of extremities. Superficial infection of incision.

(b) *The Effect on the Blood Pressure of Occlusion of the Abdominal Aorta.*—Fourteen experiments were performed in which the blood pressure in the carotid and femoral arteries was determined before, during and after the occlusion of the abdominal aorta. In twelve of these, the blood pressure was recorded continuously throughout the experiment and the animal was killed at its termination. In the remaining two experiments, the aorta was completely occluded and the animals were allowed to recover. The general condition of the two animals was observed from time to time, and studies of the determinations of the blood pressure were carried out after five and eight months.

In twelve experiments, the duration of the study varied in time from less than an hour to more than ten hours. The blood pressure

studied separately. In four experiments, however, the blood pressure was recorded continuously and the cardiac output determined repeatedly for periods as long as the general condition of the experimental animals could be maintained sufficiently well to make the observations of value.

TABLE 2.—*Effect of Exposure of the Aorta Without Ligation on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO <sub>2</sub> , per Cent by Volume	Venous CO <sub>2</sub> , per Cent by Volume	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
10/8/26 Control study, no morphine .....	14	120	103.2	19.98	14.41	5.57	45.16	50.63	131.6	2362	169	20
10/8/26 4 hours after operation, no morphine .....	14	140	103.4	20.62	13.93	6.65	45.02	47.93	162.0	2364	169	17
10/9/26 28 hours after operation, no morphine .....	14	128	102.8	19.37	12.71	6.66	45.90	52.86	154.3	2317	166	19

Protocol: 10/8/26, healthy young male dog, control studies without morphine at 3:30 p. m. at 4:30 p. m., under ether anesthesia, the distal abdominal aorta was exposed and isolated but not ligated, 9:00 p. m., four hours after completion of operation, second studies were made. 10/9/26, twenty-eight hours after operation, studies made without morphine.

TABLE 3.—*Effect of the Cardiac Output of (1) Ether Anesthesia, and (2) Exposure of the Aorta Without Ligation*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
6/1/26, 2 p. m. Control study, 1 grain morphine .....	9.1	65	100.4	13.95	6.2	7.75	15.32	91	77.49	229	110	15.4
6/1/26, 4:30 p. m. After anesthesia for 40 minutes.....	9.1	130	98.4	11.92	6.79	5.13	.....	..	70.11	1357	150.2	10.5
6/1/26, 8:45 p. m. 4 hours after anesthesia and operation..	9.1	150	98	14.88	9.12	5.76	.....	..	79.33	1577	151.3	9.2

Protocol: 6/1/26, 1:30 p. m., 1 grain of morphine. 2:00 p. m., dog completely quiet, control study. 4:30 p. m., completion of forty minutes ether anesthetic. Eye reflexes abolished. 8:45 p. m., four hours following completion of anesthesia, dog able to walk around, but unsteady. Third determinations made.

The results of these four experiments are shown in tables 4, 5, 6 and 7, and in figures 1 and 2.

(a) *The Effect on the Cardiac Output of Occlusion of the Abdominal Aorta.*—In the study of the effect of occlusion of the aorta on the cardiac output, fifty-seven determinations of the cardiac output were

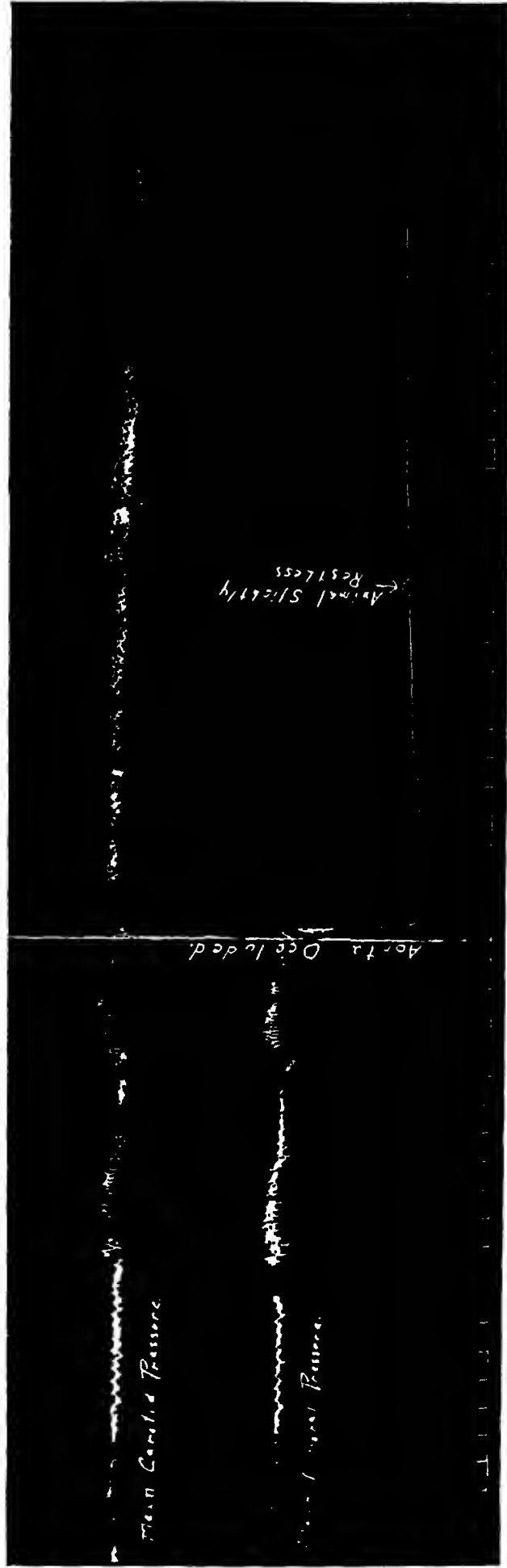


Chart 3.—A typical tracing of the blood pressures in the carotid and femoral arteries before and after occlusion of the abdominal aorta. Time was recorded in minutes. It will be noted that the carotid pressure throughout is surprisingly uniform. There is shown a slight rise immediately following occlusion of the aorta, which persists but a minute. The femoral pressure shows some slow gradual rise during the forty minutes after occlusion of the aorta. This experiment was conducted over a period of ten hours. During the remainder of the time, the carotid and femoral pressure were very constant and changed little from the level shown in the portion of the record here produced.

was found to remain relatively constant during the control period of the study. It became slightly elevated during the administration of a small amount of ether preliminary to operation. A temporary fall in blood pressure resulted from opening the abdomen and exposing the aorta. Sufficient time was allowed to elapse for the pressure to reach a constant level and then the aorta was occluded. This pressure was usually slightly lower than that which was present at the beginning of the experiment. Immediately following occlusion of the aorta, there was an average rise of 10 mm. of mercury in the carotid pressure in the nine experiments in which the mean pressure was recorded. Simultaneously, with the occlusion of the aorta, there was always a momentary stiffening of the posterior extremities. It is possible that this caused the rise in pressure. The elevation in the carotid pressure did not persist longer than two minutes in any instance. This preliminary rise in the carotid pressure was followed by a momentary decline, which in turn was followed by a slight elevation over a period of from five to ten minutes. The level reached at this time was usually maintained for several hours. In no instance was a marked subsequent rise encountered. These points are illustrated in chart 3.

Immediately after occlusion of the aorta, there was an abrupt fall in the pressure in the femoral artery. The rate of rise in the femoral pressure following the sudden decrease was variable. The greatest increase which was encountered was an elevation of 16 mm. of mercury forty minutes after the occlusion had been produced, and it remained at this level for several hours. The results of these experiments are recorded in table 17 and represented graphically in chart 4.

In the remaining two experiments, the remote effects of occlusion of the aorta on the blood pressure were studied. Recovery from the operation, in which the abdominal aorta was occluded, was uneventful in each instance except for weakness and stiffness of the posterior extremities which persisted for two and five days respectively. Both of these animals were able to use their legs in walking shortly after regaining consciousness from the anesthetic. A palpable femoral pulse was first noted in one animal four months after the ligation of the aorta. One month later, the mean carotid pressure was 150 mm. of mercury, and the mean femoral pressure 114 mm. of mercury. In the other animal, a palpable femoral pulse was detected three months after the operation. Five months later, the mean carotid pressure was 118 mm. of mercury, and the mean femoral pressure was 108 mm. of mercury. At autopsy, the terminal aorta was found to be occluded completely in both of these animals. There was no evidence of hypertrophy of the heart.

TABLE 9.—Effect of the Ligation of the Abdominal Aorta on the Cardiac Output

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO <sub>2</sub> , per Cent by Volume	Venous CO <sub>2</sub> , per Cent by Volume	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
9/11/26 Control study; no morphine..	9	75	100.6	16.10	8.28	7.82	32.72	38.49	88.5	1182	131	15
9/13/26 Control study; ¼ grain morphine .....	9	50	100.8	16.16	7.89	8.27	40.26	45.32	88.2	1066	118	19
9/17/26 Control study; ¼ grain morphine .....	8.6	70	102	15.57	8.0	7.57	42.0	43.73	81	1070	124	15
9/20/26 3 days after ligation; ¼ grain morphine .....	8.1	50	104	12.38	6.19	6.19	47.05	52.65	76.8	1241	153	22
9/24/26 ¼ grain morphine; gangrene both feet .....	7.7	125	104	9.94	3.01	6.93	47.45	52.59	81	1279	166	10

Protocol: 9/11/26, 9/13/26 and 9/17/26, control studies with and without morphine. 9/17/26, terminal aorta ligated twice and divided between ligatures. 9/20/26, dog able to walk. Looks fairly well. 9/24/26, animal has gangrene of both feet of the posterior extremities. He was killed after the determination. The gangrene was slightly more marked in the left foot. Superficial gangrene extended up into the thigh. That in the skin and subcutaneous tissues extended to a higher level than that in the muscle. There was no thrombus in the proximal end of the aorta, but there was a small one in the right iliac vessel. There was a mural antemortem thrombus on the wall of the left ventricle. Observer was unable to tell whether or not the divisions of the terminal aorta had been occluded by the ligature.

TABLE 10.—Effect of the Ligation of the Abdominal Aorta at the Trifurcation

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
1/6/26 Control study, 1 grain morphine .....	8.9	56	99	10.14	10.53	5.61	16.35	98.7	77.36	1379	155	21.6
1/8/26 24 hours after operation, 1 grain morphine.....	8.64	230	100.4	19.8	10.36	7.44	.....	.....	77.36	1039	120	4.4

Protocol: 1/6/26, control study, 1 grain of morphine. 1/7/26, aorta ligated 5 cm. above trifurcation, two lower lumbar arteries also being ligated. Dog did not give appearance of being in shock. 1/8/26, determinations made after 1 grain of morphine. Unable to walk. Condition seemed good. 1/9/26, animal died. No peritonitis, small amount of consolidation of lungs, ligatures on aorta in place.

TABLE 11.—Effect of the Ligation of the Abdominal Aorta on the Cardiac Output

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO <sub>2</sub> , per Cent by Volume	Venous CO <sub>2</sub> , per Cent by Volume	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output, per Beat, Cc.
9/27/26 Control study, 1 grain morphine .....	14.5	60	100.4	17.61	12.67	4.94	53.5	53.28	105.4	2133	147	36
9/28/26 24 hours after ligation.....	14.2	175	100	19.50	13.27	6.23	36.9	43.12	110.6	1834	129	10

Protocol: 9/27/26, control study after 1 grain of morphine. The terminal aorta was ligated twice and divided between the ligatures. 9/28/26, study after ¼ grain of morphine. Dog looked badly, not able to walk. Some swelling of the posterior extremities. 9/28/26, animal died. There was an enormous amount of swelling of the posterior extremities which extended up into the lower abdominal wall. There was no thrombus in the proximal aorta nor in the vessels below the trifurcation. No thrombus in the heart.

(c) *The Effects of Occlusion of the Abdominal Aorta on the Distribution of the Blood Volume.*—The method of study of the effects of occlusion of the abdominal aorta on the distribution of the blood volume was as follows: A dog was anesthetized with ether and securely fixed to a board which was balanced in the same manner as the platform balance. A pointer attached to one end of the board was adjusted to trace a line on a revolving kymograph. With this adjustment the respiratory movements caused the point to trace a curve on the kymograph paper similar to that obtained by the usual method of obtaining respiratory tracings. A clamp was then adjusted so that the abdominal aorta could be obstructed and released without disturbing the balance of the animal board. It was found that alternate obstruction and release of

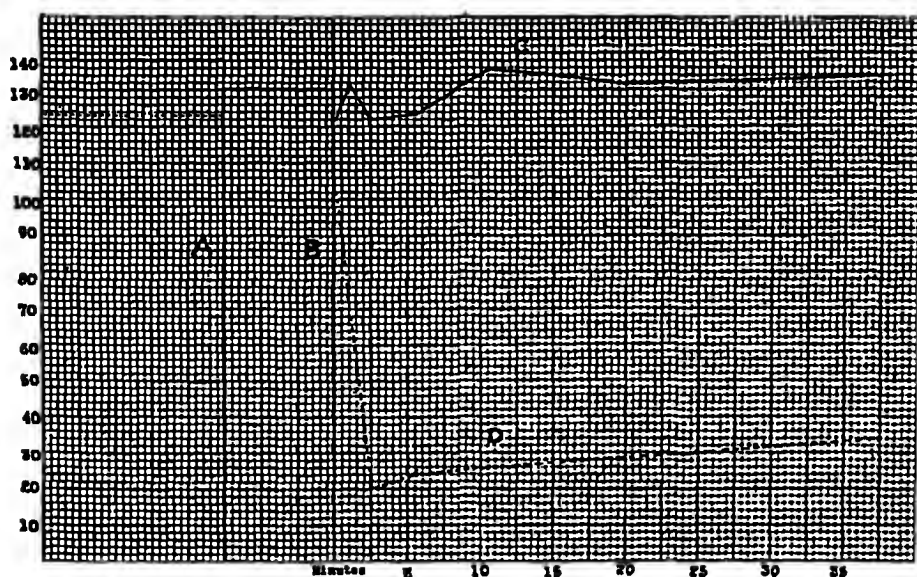


Chart 4.—The average height of blood pressure in the carotid and femoral arteries at various times during observations on the nine experiments in which the mean pressure was measured. In the control part of the experiment and after exposure of the aorta, the pressures were allowed to reach constant levels. These constant levels were measured, and their average height is shown at the left hand side of the figure. In the blood pressure tracings from these nine experiments the height of the two pressures was measured immediately after the occlusion of the aorta, also two, five, ten, twenty and forty minutes after occlusion. The average pressure thus measured is plotted accurately as to time and pressure in millimeters of mercury.

obstruction of the abdominal aorta resulted in immediate changes in the balance of the animal. Immediately after obstruction of the aorta, the end of the board toward the posterior aspect of the animal would rise. This relative change in the weights of the posterior and anterior aspects of the animal's body persisted for the entire duration of each observation. It is obvious that the nature of the conditions made it impossible



TABLE 14.—*Effect of the Ligation of the Abdominal Aorta*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O <sub>2</sub> Consumption, Cc. per Minute	<i>p<sub>H</sub></i>	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
12/9/25													
Preoperative; 1 grain morphine .....	9.55	60	100.3	16.60	10.82	5.78	18.1	91.7	77.7	7.32	1344	141	22.4
12/9/25													
4½ hours after operation .....	9.55	49	96	18.38	11.71	6.68	19.04	96.6	80.72	7.42	1210	127	21.7
12/10/25													
20 hours after operation .....	9.3	138	101.6	18.07	9.93	8.14	19.0	95.1	80.38	7.49	988	100.6	7.2
12/11/25 .....	9.0	160	102.6	16.28	10.94	5.34	16.5	98.7	86.0	....	1610	179	10.1
12/13/25 .....	8.9	135	102.7	15.34	10.71	4.63	15.54	98.7	91.4	....	1978	222	14.6
12/19/25 .....	8.18	180	104	12.91	7.62	5.29	13.78	93.7	76.8	....	1450	177	8.1

Protocol: 12/9/25, control study followed by ligation of aorta; aorta divided between two ligatures. 12/10/25, studies without morphine. Dog looks well, but cannot walk. 12/11/25, animal able to walk, looks well. 12/12/25, looks well, infection of incision line. 12/15/25, increase in amount of infection of incision, abdomen soft on palpation. 12/19/25, infection of incision about the same. Animal killed, no general peritonitis. Ligatures on aorta in place. Animal injected with bismuth sulphate, good collateral circulation shown by x-ray examination.

TABLE 15.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO <sub>2</sub> , per Cent by Volume	Venous CO <sub>2</sub> , per Cent by Volume	O <sub>2</sub> Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
8/23/26												
Control study; 1 grain morphine .....	16.2	42	100	21.32	16.1	5.22	.....	.....	126	2114	131	50
8/26/26												
1 grain morphine.....	15.9	44	98.6	18.0	13.73	4.27	.....	.....	109.5	2564	161	58
9/2/26												
1 grain morphine.....	14.7	60	101.4	17.92	12.29	5.63	43.33	47.17	126	2238	152	37
9/10/26												
1½ grains morphine.....	14.9	54	101.8	16.46	12.31	4.15	40.47	44.76	126	3036	204	56
9/20/26												
¾ grain morphine.....	15	56	101.6	18.99	14.27	4.72	43.06	49.32	166	3517	234	63
10/6/26												
5/4 grains morphine.....	15	54	100.8	17.81	13.0	4.81	53.51	58.56	122.4	2521	168	47
10/8/26												
5/4 grains morphine.....	15	56	100.4	17.55	12.69	4.86	56.89	62.17	120	2419	161	43

Protocol: 8/23/26, healthy female dog. Control study after 1 grain of morphine. The aorta was ligated twice just above the trifurcation and divided between the ligatures after the control determinations. 8/26/26, looks well. Quiet during determinations. 9/2/26, animal quiet during determinations. 9/10/26, animal fairly quiet during determinations. 9/20/26, animal restless during determinations. 10/6/26, 5/4 grains morphine. Animal quiet during determinations. Looks well. 10/8/26, 5/4 grains morphine. Animal quiet during determinations. Femoral arterial pulsations felt. O<sub>2</sub> content femoral artery was 17.19; CO<sub>2</sub> content 54.91.



the curve traced by the writing point assumed an almost constant level. If the clamp was then removed from the aorta, the weight of the posterior aspect of the animal's body became immediately greater. The amount of relative increase in weight of the posterior aspect of the animal's body was such that the writing point descended on the kymograph paper to a level lower than before the aorta was obstructed, and there was a visible hyperemia of the skin of the posterior extremities.

From the results obtained from these relatively crude experiments, it was obvious that occlusion of the abdominal aorta resulted in an immediate shifting of the blood volume from the vessels on the distal aspect of the obstruction to those proximal to the point of obstruction. This is in contrast to the generally accepted opinion that slowing of the circulation is associated with an accumulation of blood in the peripheral vessels and fluid in the tissues. It is, of course, obvious that the results obtained in these experiments are only indicative of what happens immediately after the occlusion of an artery. The relationship between edema and arterial obstruction has already been discussed in a previous publication.<sup>7</sup> It might be that the increased blood volume in the anterior part of the animal's body was contained in a dilated heart or congested pulmonary circulation, but it would seem as if such a condition would be associated with increased blood pressure in the aorta. Such is not the case. The possible importance of the changes in the distribution of blood volume immediately following occlusion of the abdominal aorta as a factor influencing the changes in the blood pressure will be discussed later.

#### COMMENT

The results of the experiments described in this paper bear particularly on the study of the effects on the heart of occlusion of the abdominal aorta. The experiments show that occlusion of the abdominal aorta results in the following changes:

1. The cardiac output is decreased.
2. There is little, if any, change in the blood pressure in the artery proximal to the occlusion.
3. Immediately following the occlusion there is a transfer of the blood volume from the distal to the proximal aspect of the obstruction.

The amount of work which is done by the heart is expressed by the following formula:  $W = Mp \text{ plus } \frac{MV^2}{2g}$  in which  $W$  is the work

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7. Brooks, Barney: Pathologic Changes in Muscle as a Result of Disturbances of Circulation: An Experimental Study of Volkmann's Ischemic Paralysis, *Arch. Surg.* 5:188 (July) 1922.

to observe the change for a long period since any movement in the animal's body operated to change the condition of balance.

The result of the release of the obstruction of the aorta was particularly interesting. If the animal was brought into a state of

TABLE 16.—*Effect of the Ligation of the Abdominal Aorta at the Trifurcation*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O <sub>2</sub> , per Cent by Volume	Venous O <sub>2</sub> , per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O <sub>2</sub> Consumption, Cc., per Minute	Cardiac Output per Minute, Cc.	Output per Kg., per Minute, Cc.	Output, per Cent, Cc.
1/14/26												
Preoperative control study..	10.2	56	.....	19.03	15.03	4.0	20.3	93.7	80.9	2022	195	36
1/15/26												
9 hours postoperative.....	10	76	.....	22.3	17.07	5.23	23.53	94.8	77.23	1476	147.6	19
1/16/26 .....	10	92	100.8	10.2	15.2	4	20.5	93.7	80.9	2022	202.2	123

Protocol: 1/14/26, control study, 1 grain morphine. 1/15/26, aorta ligated just above the trifurcation. Animal able to walk three hours following completion of the operation. X-ray examination at this time showed normal heart and lungs. Studies made nine hours following completion of the operation  $\frac{3}{4}$  grain of morphine used. 1/16/26,  $\frac{3}{4}$  grain, third series of observations made. 1/18/26, evidence of distemper. 1/21/26, animal died. X-ray examination previous to death showed pneumonia on left side and a heart of normal size. Autopsy revealed extensive pneumonia. Ligatures on aorta in place.

TABLE 17.—*Effect on (1) the Mean Carotid Blood Pressure and (2) the Mean Femoral Blood Pressure of Ligation of the Abdominal Aorta \**

Experiment Number	Date	Control Pressure		Immediately after Exposure		Immediately before Occlusion		Immediately after Occlusion		2 Minutes after Occlusion		5 Minutes after Occlusion		10 Minutes after Occlusion		20 Minutes after Occlusion		40 Minutes after Occlusion	
		Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral
41	10/ 5/26	86	88	63	68	60	68	74	51	72	0	74	0	...	...	...	...	...	...
39	9/21/26	152	114	174	120	162	114	178	151	18	174	129	...	...	...	...	...	...	...
42	11/ 0/26	...	...	132	120	91	90	93	38	74	33	59	31	...	...	...	...	...	...
40	11/ 3/26	146	138	134	118	142	128	...	...	142	...	148	...	136	...	...	...	...	...
37	9/ 8/26	144	122	164	122	114	76	132	23	128	12	124	13	118	12	130	12	...	...
41	10/21/26	162	164	142	130	148	142	154	100	140	40	145	42	158	42	...	...	...	...
36	9/ 3/26	126	126	118	90	148	112	154	29	142	32	140	28	128	...	154	31	131	31
45	10/ 2/26	160	130	130	120	130	116	133	31	126	16	120	20	...	...	...	...	...	...
47	11/ 5/26	...	...	102	104	110	91	134	20	110	12	114	16	...	...	...	...	...	...
Average...		139	124	130	110	122	101	132	43	121	21	123	21	137	26	122	28	134	31

\* This table shows the actual pressures in millimeters of mercury in the carotid and femoral arteries in nine experiments in which the mean pressure was measured. The measurements were taken during the control portion of the experiment, immediately after exposure of the aorta, immediately before occlusion of the aorta, immediately after occlusion of the aorta, and two, five, ten, twenty and forty minutes after its occlusion. The averages of these are given below. These are the figures plotted in figure 4.

balance and a clamp applied to the aorta, the posterior aspect of the animal would become relatively lighter, and the writing point at the foot of the balance board would make a tracing at a higher level on the kymograph paper. If the clamp obstructing the aorta was then allowed to remain in a position for a period of five or ten minutes,

seems possible that if the experimental animal was in a condition in which the blood pressure was low and the functioning blood volume was decreased, then obstruction of the aorta and the consequent shifting of the blood volume from the distal to the proximal aspect of the obstruction would operate to increase the blood pressure in the base of the aorta. In order to test this, some additional experiments were performed in which the effect of occlusion of the aorta in animals with low blood pressure was studied. It was found that if the blood pressure in the carotid artery was low, then occlusion of the aorta resulted in a small temporary rise of blood pressure which was apparently not different from that observed in animals in which the blood pressure was normal. If the aorta was obstructed in an animal in which the blood pressure was low and if sufficient time was allowed to elapse for the disappearance of the temporary rise in the carotid pressure, then release of the obstruction of the aorta resulted in a marked sudden fall in the carotid pressure which slowly returned to the former level. The form of the blood pressure curve, immediately after the obstruction and release of obstruction of the abdominal aorta, is such as to suggest that the changes in blood pressure on the proximal aspect of the ligature is due to the changes of the distribution of the blood volume.

of the heart,  $M$  is the mass of blood put out in a unit of time,  $P$  is the average arterial pressure and  $V$  is the velocity of the blood at the base of the aorta during ventricular expulsion. From a study of the relationship existing between the various factors of this formula, it is clear that the substitution in it of the values resulting from obstruction of the aorta would not increase the value of the factor  $W$ . The fact that blood pressure in the base of the aorta is so little altered by the relatively great changes in the conditions of the peripheral circulation which must follow the occlusion of so large a vessel, as the abdominal aorta, is evidence of the importance of the vagopressor reflex which operates to keep the arterial blood pressure constant in the presence of alterations in venous pressure and cardiac output.

The fact that the conclusions reached in this study are contradictory to those of Katzenstein deserves a word of comment. From a study of the experiments described in this paper and those described by Katzenstein, it is clear that the effects on the blood pressure observed immediately after obstruction of the aorta are not essentially different. In Katzenstein's experiments, the most marked elevations of blood pressure observed and attributed to the effect of ligation of the aorta were in instances in which the intra-arterial tension was determined before the aorta was ligated, and then again after periods of from three days to four weeks.

In the experiments described in this paper, great care was taken to observe the effects of occlusion of the abdominal aorta under conditions of the circulation which were as nearly normal as possible. From a study of the protocols of the experiments described by Katzenstein, it appears that in at least some of his experiments the blood pressure was abnormally low at the time the aorta was obstructed. Most of his experiments were conducted on animals anesthetized with chloroform. This anesthetic produces marked effects on the blood pressure. Some of Katzenstein's experiments were performed on animals paralyzed with curare. Although this drug apparently does not have any effect on the blood pressure, it is probable that the experimental animal under the influence of curare is in a condition in which other factors produced changes in blood pressure which would not occur if this drug had not been administered.

In the experiments conducted for this study in which the experimental animals were examined after relatively long periods had elapsed since the occlusion of the aorta, no evidence was found of hypertrophy of the heart.

It was thought that the shifting of the blood volume in the animal's body might account for some of the changes in the blood pressure observed to follow ligation of the abdominal aorta. For example, it

of their concentrations, expressed in milligrams per hundred cubic centimeters of serum, equalled a certain minimal figure, which lay roughly between 30 and 40.

In 1924, Petersen<sup>5</sup> studied a series of clinical cases of nonunion, and a series of dogs after experimental fracture. He believed that the underlying basis of many cases of nonunion was made manifest in a deficiency in either a subnormal calcium or an inorganic phosphorus content of the serum. He used the calcium and phosphorus product advocated by Howland and Kramer to show this deficiency. He found the optimum product for healing to be between 35 and 40, while products less than 30 were the rule in patients with nonunion.

Since our work was carried out on patients suffering with fractures at diversified sites, it seemed necessary to obtain for study a series of cases in which the fractures occurred at the same site and were produced in the same way in persons of approximately the same age. It was necessary, therefore, to utilize an experimental animal for this work.

We wished to ascertain: (1) whether ossification would occur in a shorter period of time in the normal animal after the administration of parathyroid extract-Collip, which increases calcium retention in the blood, than in the normal control animal; (2) whether cod liver oil alone, which increases phosphorus and sometimes calcium retention in the rachitic animal, would have any beneficial effect on ossification in the normal animal; and (3) whether union would occur after a considerable fall in the serum calcium, as is found after thyroparathyroidectomy.

#### EXPERIMENTAL WORK

Small young dogs were used for this work. The site selected for fracture was the radius, just below the middle of the shaft. The bone was exposed and fractured with a chisel. After fracture, the wound was closed and a molded aluminum splint was applied. All operations were performed under careful aseptic technic and no infections occurred. The dogs were healthy stock animals, of about the same age, but they did not belong to the same litter. They were kept on a diet of dog biscuits and milk, and were given as much as they would eat.

Fracture was produced in: (1) normal control dogs, (2) dogs receiving 20 cc. of cod liver oil daily, (3) dogs in which the serum calcium level was raised by the administration of parathyroid extract-Collip and (4) dogs in which the serum calcium level was lowered by thyroparathyroidectomy.

The last mentioned animals were prepared for thyroparathyroidectomy by the method of Jones,<sup>6</sup> i. e., feeding 20 cc. of cod liver oil daily, beginning two weeks before the removal of the glands. Only one dog lived until union of the fracture was complete. This one was in excellent condition and was killed 186 days after thyroparathyroidectomy.

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5. Petersen, Henry A.: *J. Bone & Joint Surg.* 22:885, 1924; *Bull. Johns Hopkins Hosp.* 35:378, 1924.

6. Jones, J. H.: *J. Biol. Chem.* 70:647, 1926.

# OSSIFICATION AFTER FRACTURE

## AN EXPERIMENTAL STUDY \*

I. S. RAVDIN, M.D.

AND

MARY E. MORRISON, M.S.

Jacob Randolph Fellow in Research Surgery

PHILADELPHIA

In 1926, one of us (I. S. R.) with Jonas<sup>1</sup> studied the serum calcium and inorganic phosphorus in a series of patients with fractures at diversified sites. From this study we were doubtful as to whether the serum calcium and inorganic phosphorus content in clinical cases could be used as a prognostic index for union or nonunion in the majority of instances.

In 1924, Shipley<sup>2</sup> investigated conditions under which calcification occurred in vitro. He found that in slabs of completely rachitic bones, incubated in normal serum, calcification occurred promptly, whereas sections of the same bone in rachitic serum failed to calcify. In 1926, Shipley, Kramer and Howland<sup>3</sup> repeated and confirmed Shipley's results, and showed, also, that calcification occurred promptly in slabs of rachitic bone incubated in solutions of inorganic calcium and phosphorus in concentrations similar to those of normal serum. It was their opinion that failure to produce calcification in vivo was dependent on an insufficient concentration of calcium and inorganic phosphorus in the fluids around the growing bone. Remarkable as it may seem, these investigators found that calcification in vitro occurred within from sixteen to twenty-four hours when the concentrations of inorganic calcium and phosphorus were 7 and 5 mg., respectively, per hundred cubic centimeters as well as when they were 10 and 3.5 mg., respectively.

In 1922, Howland and Kramer<sup>4</sup> published the results of a study of the calcium and phosphorus of the serum in children with rickets and in those with rickets complicated by tetany. They believed that the determining factor in the calcification of bone in these cases was the presence of calcium and phosphorus in such amounts that the product

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\* From the Laboratory of Surgical Research and the William Pepper Laboratory, University of Pennsylvania.

1. Ravdin, I. S., and Jonas, L.: *Ann. Surg.* **34**:37, 1926.

2. Shipley, P. G.: *Bull. Johns Hopkins Hosp.* **35**:304, 1924.

3. Shipley, P. G.; Kramer, Benjamin, and Howland, John: *Biochem. J.* **20**: 379, 1926.

4. Howland, John, and Kramer, Benjamin: *Tr. Am. Pediatr. Soc.* **34**:24, 1922.



in mols; column 3, the serum inorganic phosphorus in milligrams per hundred cubic centimeters; column 4, the serum inorganic phosphorus in mols; column 5 the calcium and phosphorus product, advocated by Howland and Kramer<sup>4</sup> and later by Petersen,<sup>5</sup> and column 6, the  $(\text{PO}_4\equiv)$  in mols (determined according to Holt, La Mer, and Chown.<sup>9</sup> In columns 6 and 7, we assume a  $p_{\text{H}}$  of 7.4. Column 7 shows the  $\text{Ca}_3(\text{PO}_4)_2$  ion product and column 8, the negative logarithm of the  $\text{Ca}_3(\text{PO}_4)_2$  ion product, as advocated by Holt.<sup>10</sup> Holt<sup>10</sup> concluded that

TABLE 2.—Calcium and Phosphorus Values Immediately Before and After Fracture, and at Union

Dog	1	2	3	4	5	6	7	8						
	Ca, Mg. per 100 Cc.	(Ca++) Mols per Liter	P, Mg. per 100 Cc.	(P) Mols per Liter	Ca x P, Mg. per 100 Cc.	(PO <sub>4</sub> ≡) Mols per Liter	(Ca++) <sup>3</sup> (PO <sub>4</sub> ) <sub>2</sub>	-Log. Prod. (P Prod.) Union, Days	Average					
Normal Controls														
36 a.	11.6	2.89	10.3	9.9	0.93	10.3	33.6	6.60	10.70	10.25	23.97	30	37.5	
b.	11.4	2.85		2.5	1.13		59.9	8.12	15.55		23.81			
c.	11.0	2.77		3.6	1.15		39.0	8.27	14.56		23.84			
48 a.	10.9	2.72		3.8	1.22		41.4	8.77	15.46		23.81	45	37.5	
b.	11.3	2.82		3.5	1.13		39.6	8.12	14.76		23.83			
c.	10.9	2.72		3.3	1.06		35.9	7.62	11.68		23.93			
Cod Liver Oil Controls														
10 a.	11.5	2.87		3.6	1.15		41.4	8.27	16.14		23.79	36	37.5	
b.	10.7	2.67		3.0	0.97		32.1	6.97	9.22		24.04			
c.	11.8	2.94		3.3	1.06		38.9	7.62	14.70		23.89			
22 b.	11.7	2.92		4.7	1.51		55.0	10.86	29.39		23.59	39	37.5	
c.	10.5	2.62		4.5	1.45		47.3	10.43	19.58		23.71			
Hypercalcemic														
12 a.	13.2	3.29		5.1	1.64		67.0	11.79	49.48		23.31	15	30	
b.	12.5	3.12		4.9	1.58		61.3	11.36	39.22		23.41			
c.	16.0	3.99		5.1	1.64		81.6	11.78	68.14		23.05			
60 b.	17.0	4.24		3.0	0.97		51.0	6.97	37.03		23.43	45	30	
c.	16.8	4.19		2.9	0.93		48.7	6.60	32.97		23.46			
Hypocalcemic														
17 a.	7.8	1.93		6.9	2.22		53.8	15.06	18.84		23.73	71	30	
b.	8.2	2.05		7.2	2.33		59.0	16.08	23.93		23.62			
c.	4.1	1.02		8.1	2.61		33.2	18.77	3.81		24.41			

the ion product,  $(\text{Ca}^{++})^3 \times (\text{PO}_4\equiv)^2$ , is a more accurate criterion of the rate of deposition of  $\text{Ca}_3(\text{PO}_4)_2$  than is the empiric  $\text{Ca} \times \text{P}$  product.

It can be seen that the calcium and phosphorus product, or the  $\text{Ca}_3(\text{PO}_4)_2$  ion product, or the negative logarithm of the  $\text{Ca}_3(\text{PO}_4)_2$  ion product could not have been used as a prognostic index for the rate of ossification in these experiments. Although in dog 12 the ion product

9. Holt, L. Emmett; La Mer, Victor K., and Chown, Bruce H.: J. Biol. Chem. 64:509, 1925.

10. Holt, L. Emmett: J. Biol. Chem. 64:579, 1925.

Calcification was followed by x-ray pictures the tenth day after fracture and as nearly as possible every week thereafter.

The serum calcium was determined by the method of Kramer and Tisdall,<sup>7</sup> and the serum inorganic phosphorus by the method of Fiske and Subbarow.<sup>8</sup> Estimations were made every two weeks, except in the hypercalcemic and hypocalcemic dogs, on whom estimations were made more frequently in an attempt to more carefully follow the levels.

### RESULTS

Table 1 gives the x-ray observations. This work was done by Dr. Henry Pancoast of the Hospital of the University of Pennsylvania.

TABLE 1.—*Report on X-Ray Observations*

Number Days After Fracture	Normal Controls		Cod Liver Oil Controls		Hypercalcemic		Hypocalcemic		
	No. 36	No. 48	No. 10	No. 22	No. 12	No. 60	No. 17	No. 27	No. 15
10	Slight periosteal reaction	No callus	.....	Very slight callus	.....	Very slight callus	Very slight callus	No evi- dence of callus	No callus
17	.....	No callus	Very slight callus	Consi- derable callus	Union	Slight periosteal callus	Slight callus	No callus	
21	More callus	Slight callus formation	Slight callus formation	.....	.....	Some increase in callus	.....	Death	
31	Union	More external callus	More callus	.....	.....	.....	Slight increase in callus	.....	Slight callus
38	.....	Consi- derably more callus	Union	Union with exces- sive exter- nal callus	.....	More callus	More callus	.....	Death
45	.....	Union	.....	.....	.....	Union	Considerable external but very little intermedi- ate callus		
52	.....	.....	.....	.....	.....	.....	Increase in external callus		
66	.....	.....	.....	.....	.....	.....	Almost united		
71	.....	.....	.....	.....	.....	.....	Union		

The x-ray examination coincided closely with the physical examination of the extremity and at the time that the roentgen-ray picture showed union, the animal was able to walk without a limp. The number of days in this table is not absolute. Several vary as much as two or three days. In dogs 15, 22 and 36, certain plates unfortunately were lost.

Table 2 shows the calcium and phosphorus values (*a*) immediately before fracture, (*b*) immediately after fracture and (*c*) at the time of union. Column 1 shows the serum calcium content in milligrams per hundred cubic centimeters; column 2, the serum calcium content

7. Kramer, B., and Tisdall, F. F. *J. Biol. Chem.* **47**:475, 1921. T. 1:23, F. 1:1.  
*J. Biol. Chem.* **56**:439, 1923.

8. Fiske, Cyrus H., and Subbarow, Yellapragada. *J. Biol. Chem.* **66**:375, 1927.

and partly as tricalcium phosphate. The enzyme (phosphoric esterase) hydrolyses the ester, and liberates inorganic phosphorus which is deposited as  $\text{Ca}_3(\text{PO}_4)_2$ . This theory is enticing, but as yet sufficient evidence has not been forthcoming to substantiate the fact that a deficient amount of esterase may account for some of the cases of nonunion after fracture.

In our own cases union occurred in every instance, with the exception of two animals (hypocalcemic) who did not live a sufficiently long time for ossification. In the one dog in which the serum calcium content was maintained at an abnormally low level, but whose phosphorus level had increased above normal, union occurred although it took approximately twice the average normal time. Surely if a low calcium content in itself is the cause of nonunion, it should have occurred in this animal. A deficient serum calcium in this case, however, produced delayed union. There is, however, the question as to whether or not a deficient serum calcium produced other than by thyroparathyroidectomy may result in nonunion. On this subject, we have no experimental data. We have not entered into a discussion of the diffusible and nondiffusible calcium in these animals.

#### SUMMARY

1. A study of the serum calcium and inorganic phosphorus after fractures in normal, hypercalcemic and hypocalcemic dogs is presented.
2. We have not been able to prognosticate the rate of ossification after fracture from the calcium and phosphorus product, from the ion product or from the negative logarithm of the ion product.
3. The marked decrease in serum calcium after thyroparathyroidectomy retarded ossification, although it did not prevent union.

#### PROTOCOLS

*Dog 36.*—Control (without cod liver oil).

March 21: Serum—Inorganic phosphorus = 2.9 mg. per hundred cubic centimeters.

Calcium = 11.6 mg. per hundred cubic centimeters.

March 23: Radius fractured.

April 2: X-ray picture showed slight periosteal reaction.

April 4: Serum—Inorganic phosphorus = 3.5 mg.

Calcium = 11.4 mg.

April 13: Serum—Inorganic phosphorus = 3.6 mg.

Calcium = 11.5 mg.

April 16: X-ray picture showed good external callus.

April 23: X-ray picture showed considerable callus with union.

*Dog 48.*—Control (no cod liver oil).

March 28: Serum—Inorganic phosphorus = 3.8 mg. per hundred cubic centimeters.

Calcium = 10.9 mg. per hundred cubic centimeters.

is higher than in the other animals, it should be remembered that this product is to the negative twenty-fifth power, so that the actual difference is exceedingly small. The ion product in dog 17 was higher for a time than that of the control dogs, yet ossification took nearly twice as long.

In the control animals and in those fed on cod liver oil, ossification occurred within approximately the same period of time.

In the hypocalcemic animals, evidence of callus was not found in one dog after sixteen days; very slight callus was found in one dog after twenty-seven days; in the third animal, union was obtained in seventy-one days.<sup>11</sup>

Greenwald,<sup>12</sup> in 1926, and Hunter and Aub,<sup>13</sup> in 1927, found an increased excretion of calcium after the administration of parathyroid extract-Collip. The amount of calcium lost could have come only from the bones. Dog 60, which required forty-five days for union, refused food for some days when the serum calcium was maintained at a level of 18 or 19 mg. per hundred cubic centimeters, and only after reduction of the serum calcium did he again eat. It is possible that, on the inadequate diet, enough calcium was drained from the bones to delay ossification. It is our opinion that parathyroid extract should be used with caution in cases of fracture.

#### COMMENT

It is highly improbable that any single factor is the cause of nonunion in the majority of instances. In one instance it may be due to the interposition of soft parts; in another, to an inefficient blood supply at the site of fracture due to injury or location; in another, to damage to the periosteum, and in still another, it may be due to an insufficient amount of the inorganic constituents of the blood which take part in ossification.

Although a deficient inorganic phosphorus or calcium content of the serum may be the cause of abnormal or faulty ossification in the growing bone or in certain of the bone dyscrasias, it has been our experience that this factor is a rare one in the clinical patient with nonunion after fracture.

Robison<sup>14</sup> advanced the theory that calcification depends on the activity of an enzyme secreted by the osteoblasts and hypertrophic cartilage cells. He stated the belief that calcium and phosphorus exist in the blood and other tissue fluids partly as calcium phosphorus ester-

June 2: X-ray picture showed very slight callus.

June 6: Serum—Inorganic phosphorus = 3.3 mg.

Calcium = 11.8 mg.

X-ray picture showed slight callus formation.

June 11: X-ray picture showed more callus.

June 20: X-ray picture showed considerable external callus with union.

Dog 22.—Cod liver oil control.

April 27: Fractured radius.



Fig. 2 (dog 48).—*A* shows the bone ten days after fracture; *B*, forty-five days.

April 29: Serum—Inorganic phosphorus = 4.7 mg. per hundred cubic centimeters.

Calcium = 11.7 mg. per hundred cubic centimeters.

May 7: X-ray picture showed very slight callus.

May 13: Serum—Inorganic phosphorus = 5.8 mg.

Calcium = 11.7 mg.

May 14: X-ray picture showed considerable external callus.

May 28: Serum—Inorganic phosphorus = 4.5 mg.

Calcium = 11.2 mg.

June 5: X-ray picture showed union with considerable external callus.

March 30: Fractured radius.

April 6: No callus.

April 11: Serum—Inorganic phosphorus = 3.5 mg.  
Calcium = 11.3 mg.

April 16: No callus.

April 25: Serum—Inorganic phosphorus = 3.3 mg.  
Calcium = 11.9 mg.

X-ray picture showed slight callus formation.

April 30: X-ray picture showed more external callus.



Fig. 1 (dog 36).—*A* shows the bone ten days after fracture; *B*, thirty days.

May 7: X-ray picture showed considerably more callus.

May 9: Serum—Inorganic phosphorus = 3.3 mg  
Calcium = 10.9 mg.

May 14: X-ray picture showed union.

Dog 10.—Cod liver oil control.

May 13: Serum—Inorganic phosphorus = 3.6 mg per hundred cubic centimeters.

Calcium = 11.5 mg per hundred cubic centimeters.

Fracture of radius.

May 25: Serum—Inorganic phosphorus = 3.3 mg  
Calcium = 10.7 mg

*Dog 12.*—Hypercalcemic.

Feb. 21: Serum—Inorganic phosphorus = 5.2 mg. per hundred cubic centimeters.

Calcium = 11.8 mg. per hundred cubic centimeters.

March 7: Serum—Inorganic phosphorus = 4.6 mg.

Calcium = 11.5 mg.

10 units parathyroid extract.

March 9: Serum—Inorganic phosphorus = 5 mg.

Calcium = 14 mg.

10 units parathyroid extract.



Fig. 5 (dog 12).—Fifteen days after fracture.

March 11: Serum—Inorganic phosphorus = 4.9 mg.

Calcium = 11.8 mg.

10 units parathyroid extract.

March 14: Serum—Inorganic phosphorus = 5 mg.

Calcium = 11.3 mg.

30 units parathyroid extract.

March 16: Serum—Inorganic phosphorus = 5.1 mg.

Calcium = 13.2 mg.

40 units parathyroid extract.



Fig. 3 (dog 10).—Thirty-six days after fracture.





- April 11: Dog in splendid condition.  
Serum—Inorganic phosphorus = 7.3 mg.  
Calcium = 7.7 mg.  
X-ray picture showed slight external callus.
- April 23: Slight increase in external callus.
- April 25: Condition splendid.  
Serum—Inorganic phosphorus = 8.8 mg.  
Calcium = 5.4 mg.
- April 30: Further increase in external callus.

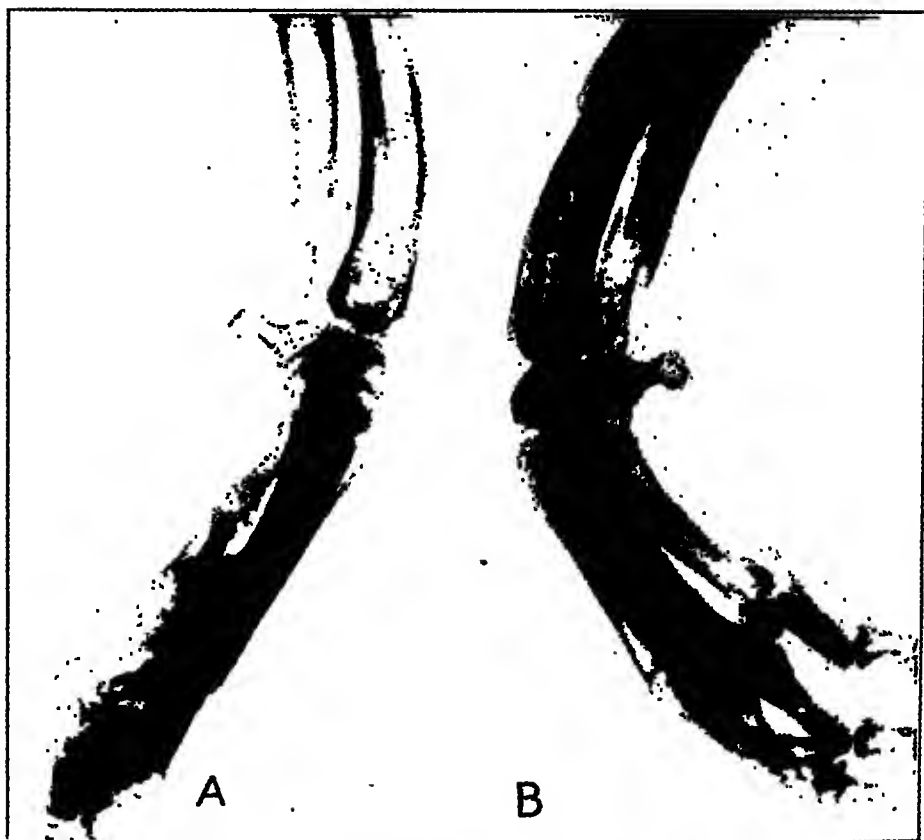


Fig. 8 (dog 27).—*A* shows the bone ten days after fracture; *B*, sixteen days.

- May 7: X-ray picture showed considerable external callus.
- May 14: X-ray picture showed increase in external callus.
- May 28: X-ray picture showed fracture almost united.
- June 1: Excellent condition.  
Serum—Inorganic phosphorus = 8.1 mg.  
Calcium = 4.1 mg.
- June 4: X-ray picture showed union.  
Dog killed 186 days after operation. Condition excellent.
- Dog 27.*—Hypocalcemic.
- Feb. 7: Started feeding 20 cc. cod liver oil daily.

March 18: Serum—Inorganic phosphorus = 4.9 mg.

Calcium = 12.5 mg.

50 units parathyroid extract.

Fracture of radius.

March 19 and 21: 50 units parathyroid extract each day.

March 23: Serum—Inorganic phosphorus = 4.8 mg.

Calcium = 11.9 mg.

March 25 and 27: 100 units parathyroid extract each day.

March 28: Serum—Inorganic phosphorus = 5.1 mg.

Calcium = 16 mg.

March 30: 10 units parathyroid extract.

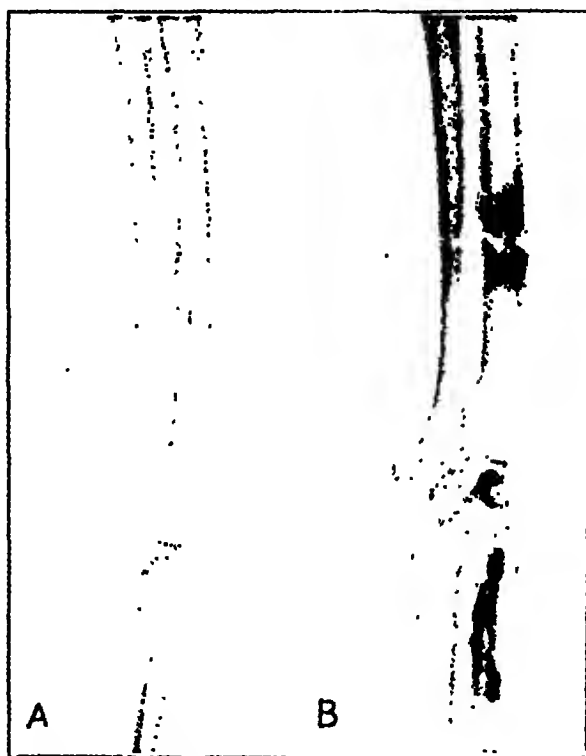


Fig. 6 (dog 60).—A shows the bone ten days after fracture; B, forty-five days.

March 31: 40 units parathyroid extract.

April 1: Serum—Inorganic phosphorus = 13.4 mg.

Calcium = 4.7 mg.

April 2: X-ray picture showed definite evidence of union. Dog able to walk without limp, no crepitation.

Dog 60.—Hypercalcemic.

April 19: 100 units parathyroid extract.

April 20: Serum—Inorganic phosphorus = 3 mg. per 100 cc. of blood; calcium = 17 mg. per 100 cc. of blood.

Fracture of radius.

March 25: X-ray picture did not show evidence of callus. Died after considerable loss of weight from lack of food. No attempt was made to force diet. Animal was not in tetanic spasm since March 2.

*Dog 15.*—Hypocalcemic.

April 16: Started feeding 20 cc. cod liver oil daily.

May 2: Thyroparathyroidectomized.

May 4: Serum—Inorganic phosphorus = 7.5 mg. per hundred cubic centimeters.

Calcium = 8.2 mg. per hundred cubic centimeters.

May 4: Fracture of radius.

May 6: Serum—Inorganic phosphorus = 7.8 mg.

Calcium = 5.9 mg.

May 11: Condition fair. Slight weakness and eyes sore-looking. No sign of tetany.

Forced feeding of milk but not much food retained.

Serum—Inorganic phosphorus = 8.7 mg.

Calcium = 5.3 mg.

May 13: Weak, blind from bilateral cataract. No tetany.

Given 20 units of parathyroid extract.

May 14: X-ray picture did not show evidence of callus.

May 18, 9 a. m.: Very good condition now, except for sore eyes.

Drank milk voluntarily.

11 a. m.: Severe attack of tetany.

Given 20 units of parathyroid extract.

May 20: Condition better.

May 23: Condition considerably improved.

May 25: Severe conjunctivitis.

May 26: Eyes in bad condition.

Serum—Inorganic phosphorus = 7.5 mg.

Calcium = 3.3 mg.

May 30: Slight callus.

May 31: Died after gradual loss of weight and inanition. No tetany.

Feb. 25: Serum—Inorganic phosphorus = 3.1 mg. per hundred cubic centimeters.

Calcium = 10.2 mg. per hundred cubic centimeters.

Feb. 28: Thyroparathyroidectomized.

March 2: In tetany.

Gave cod liver oil and 20 units of parathyroid extract.

March 4: Shivering. Gave 10 units of parathyroid extract.



Fig. 9 (dog 15).—*A* shows the bone ten days after fracture; *B*, twenty-seven days.

March 7: Serum—Inorganic phosphorus = 4 mg. Animal not in tetany, but not in good condition.

Calcium = 5 mg.

Condition improved.

March 9: Fractured radius and ulna.

March 11: Serum—Inorganic phosphorus = 3.9 mg.

Calcium = 5.3 mg.

Poor condition; not eating.

March 13: Poor condition. Not eating his food.

Put on diet of anything he would eat. No improvement.

March 15: X-ray picture of the leg was taken. Fracture of radius and ulna.

*Operation.*—The usual laminectomy procedure was carried out. The fifth, sixth, and seventh dorsal spinous processes were removed. There was no extra dural fat. The dura did not pulsate, and at the place where there was a fusiform enlargement, the dura had a yellowish tinge, as shown in figure 1 *A*. When the dura was opened, the cord was found distended by a yellowish mass beneath the arachnoid which had running over it fine longitudinal bands of tissue from the spinal cord. The appearance is well illustrated in figure 1 *B*. A longitudinal incision was made over this mass after one vessel that ran over the cord had been clipped. Careful retraction of the incised tissue finally revealed an encapsulated lipoma which was readily peeled out of the substance of the cord (fig. 1 *C*).

After the tumor had been removed, a shallow ovoid cavity remained in the cord. As the field was perfectly dry, the dura was closed with fine silk and the wound was closed in layer sutures in the usual way.

*Discharge.*—The patient was discharged from the hospital two weeks after operation. There was spasticity of the lower extremities just as there had been before operation, but he was able to walk with the aid of a cane.

*Pathologic Examination.*—The tumor weighed 2.25 Gm., was 2.5 cm. long and 1 cm. in diameter; it was nodular, encapsulated, moderately firm and whitish-yellow. Sections from different parts of the specimen showed that it was composed entirely of fat tissue (fig. 2). There were few small blood vessels, but one large one was found in every section. The capsule of the tumor was moderately thick and was composed of a dense connective tissue (fig. 3). Specific stains on sections from different areas of the tumor did not show neural or glial elements.

#### COMMENT

A more definite conception of the rarity of intramedullary lipomas of the spinal cord may be gained from their incidence in the large collections of tumors of the cord reported by various authors. In the well known monograph by Gowers and Horsley<sup>1</sup> on the first successfully removed tumor of the spinal cord, the authors reported fifty-eight cases collected from the literature. The occurrence of an intramedullary lipoma is not recorded by them.

In 100 tumors studied by Elsberg,<sup>2</sup> fourteen were intramedullary. Not one of the fourteen was a lipomatous growth. Steinke<sup>3</sup> collected reports of 330 tumors of the cord for Frazier, and no case of intramedullary lipoma is found in this large group.

In a series of 112 laminectomies reported by Adson and Ott<sup>4</sup> for focal symptoms of disease of the cord, not a single case of lipoma within the cord was found. In 156 laminectomies performed at Barnes Hos-

1. Gowers, W. R., and Horsley, V.: A Case of Tumor of the Spinal Cord; Removal; Recovery, *M. Chir. Trans.*, London, 1888, vol. 71, p. 377.

2. Elsberg, Charles: Tumors of Spinal Cord, New York, Paul B. Hoeber, Inc., 1925.

3. Steinke, C. R.: Spinal Tumors. Statistics on a Series of 330 Collected Cases, *J. Nerv. & Ment. Dis.* 47:418, 1918.

4. Adson, A. W., and Ott, W. O.: Results of Removal of Tumors of the Spinal Cord, *Arch. Neurol. & Psychiat.* 8:520 (Nov.) 1922.

# INTRAMEDULLARY LIPOMA OF THE SPINAL CORD

## COMPLETE OPERATIVE REMOVAL \*

ERNEST SACHS, M.D.

AND

EDGAR F. FINCHER, Jr., M.D.

Fellow of the National Research Council

ST. LOUIS

Intramedullary lipoma of the spinal cord is extremely rare clinically. Because of its rarity and also because it was possible to remove the tumor at operation, it has been deemed desirable to report this case.

### REPORT OF A CASE

*History.*—J. M., a man, aged 46, entered Barnes Hospital in February, 1928, complaining of weakness in the lower extremities. The onset occurred three years prior to entrance, with pain in both ankles and in the right knee. Although pain was without relation to motion, he was treated for arthritis for six months. When not standing, he was free from discomfort. Weakness soon intervened, and he had been incapacitated for work during the past eighteen months of his illness. A year before he entered the hospital, the pain had almost subsided but weakness gradually progressed, so that walking was possible only with considerable difficulty. The outstanding feature was an inability to lift his feet. Marked subjective sensory disturbances or altered bladder or rectal function had never been present.

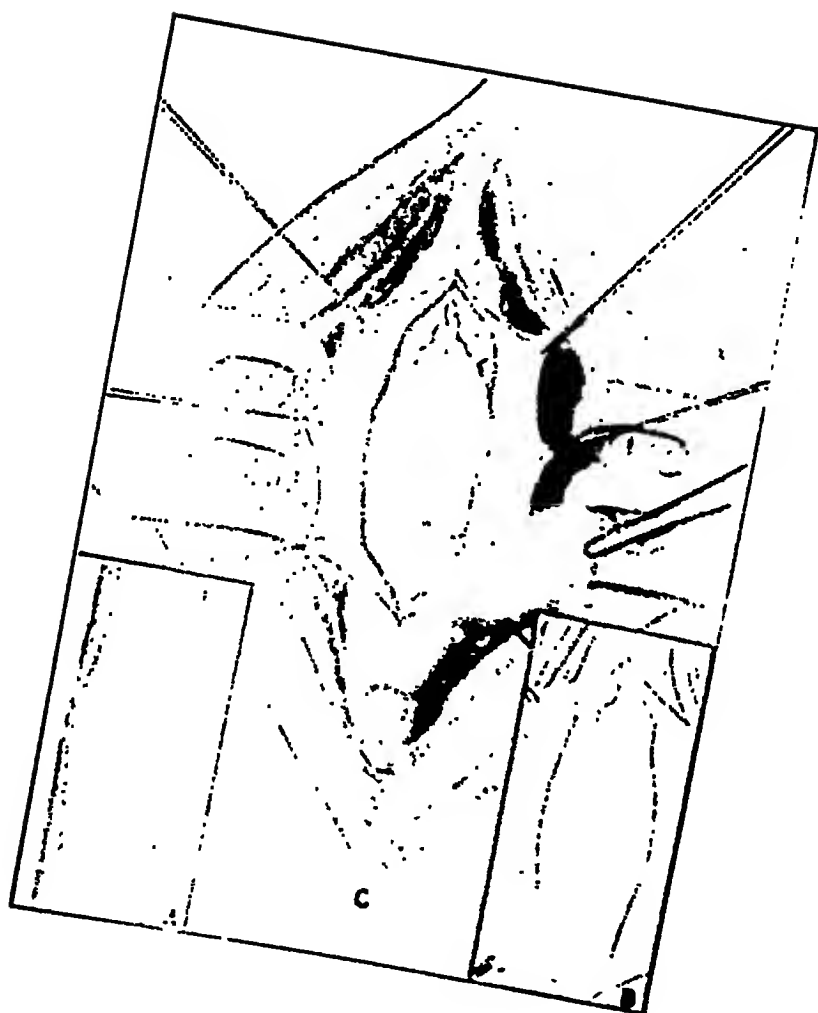
*Examination.*—There was a diminution in sensation to light touch, pinprick, heat and cold, from the twelfth dorsal skin segment down. A band of complete anesthesia, corresponding to the tenth and twelfth dorsal skin segment, was present. The abdominal reflexes were absent and the cremasteric reflexes rather feeble. The patellar and ankle jerks were increased. A bilateral Oppenheim sign was elicited. There was a slight spasticity of the lower extremities, but patellar or ankle clonus was not present. The rest of the physical examination gave negative results.

*Diagnosis.*—Lumbar puncture with a water manometer showed a spinal fluid pressure of 19 cm. Ten-second bilateral jugular compression increased the fluid pressure to 29 cm. When the jugular pressure was released, the spinal fluid returned to 19 cm. within ten seconds. The fluid came out in a normal or a steppage fashion. This was interpreted as a partial block of the spinal fluid. Laboratory examination of the fluid was normal throughout.

Later, an injection of iodized oil 40 per cent was made. X-ray examination showed that the greater part of the 1.5 cc. of oil, upon injection of which had been made into the cisterna magna, had dropped to the bottom of the cisterna. However, in the mid-dorsal region, streaks of oil were believed to be present. The point at which the phantoms were believed to correspond to the lesion as determined by neurological examination.

\* From the Neurosurgical Service, Department of Surgery, Barnes Hospital, University School of Medicine and Barnes Hospital.







to accept Wolbach's idea that this tumor was associated with a spina bifida. In Turner's case, the description is that of a fibronuclear tumor containing fat cells and was considered by him a sarcomatous growth. Wolbach prefers the term diffuse subdural lipomatosis of the spinal cord in his case. In view of the fact that this was associated with other congenital anomalies, it seems probable to us, as it did to the author, that this was just another congenital defect.

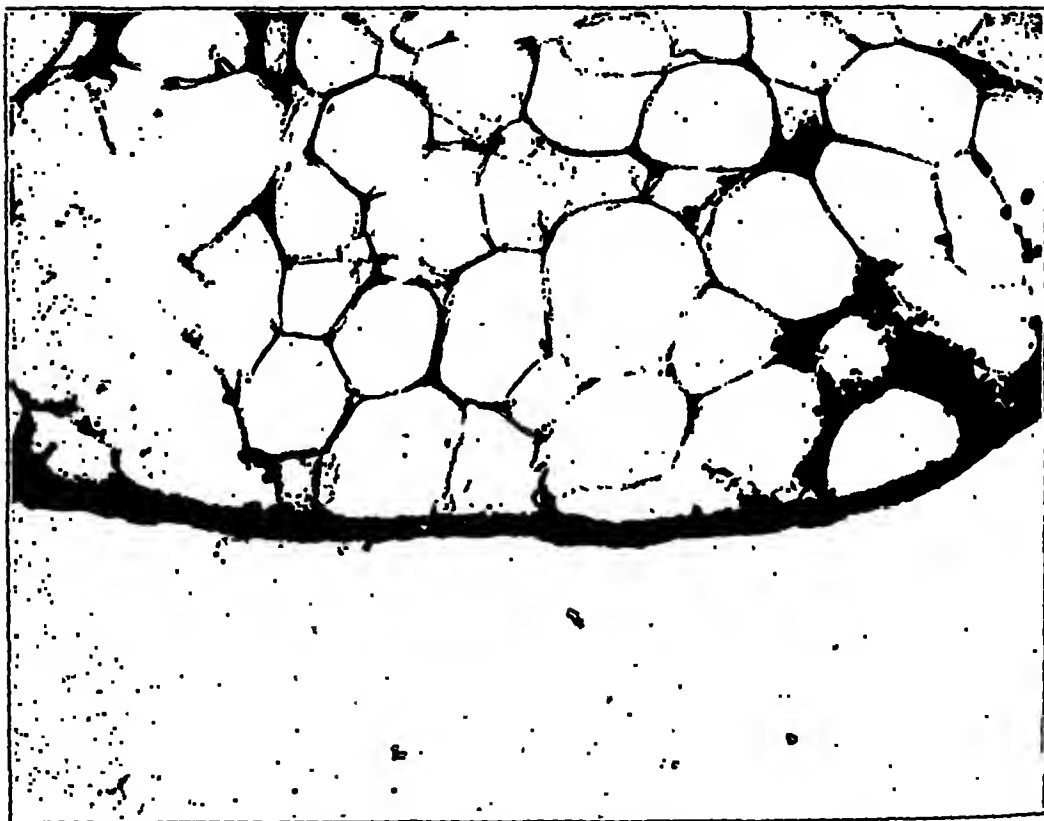


Fig. 3.—Capsule that entirely surrounded the tumor. Phosphotungstic acid stain;  $\times 300$ .

In the remaining seven cases from the literature (Branbach,<sup>9</sup> Spiller, Thomas,<sup>10</sup> Ritter,<sup>11</sup> Stookey,<sup>5</sup> Oppenheim and Borchardt<sup>12</sup> and

9. Branbach: Ein fall von Lipom bildung der Rückenmarks häute, Arch. f. Psychiat. 15:489, 1899.

10. Thomas, S., and Jumentie, J.: Lipome de cone terminale, Rev. neurol. 21: 222, 1912.

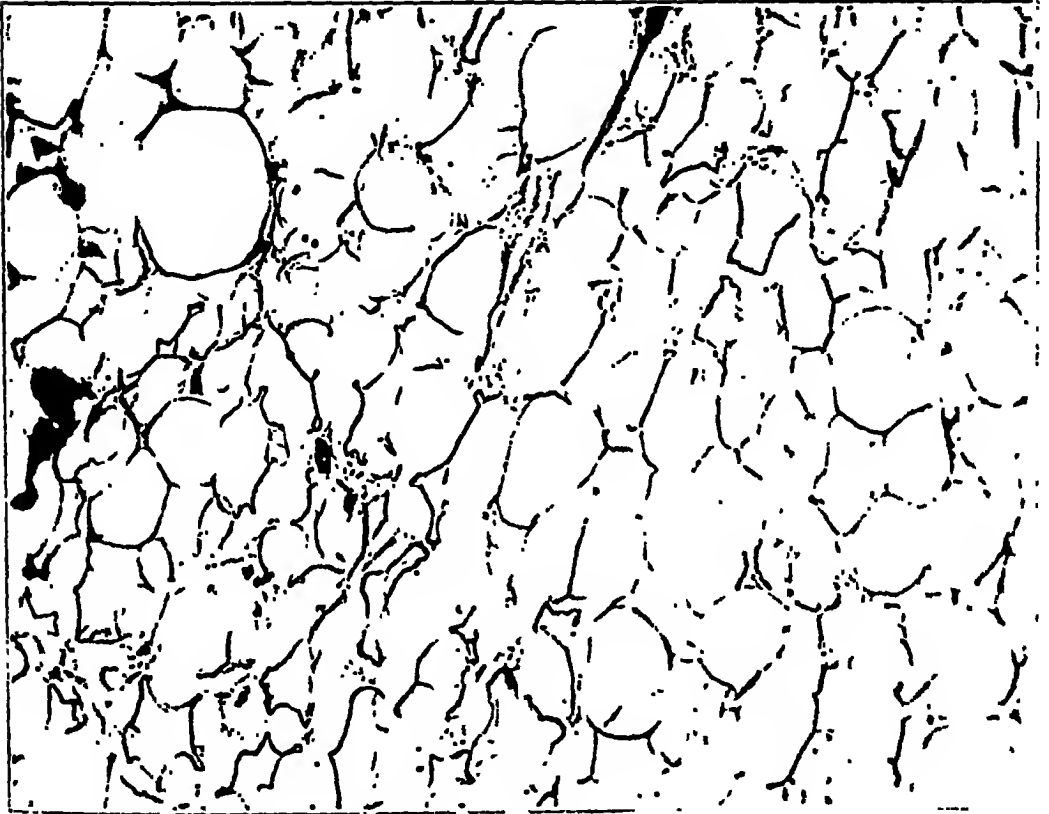
11. Ritter, A.: Ein Lipoma der Meningen des Cervicalmarks, Deutsche. Ztschr. f. Chir. 152:189, 1920.

12. Oppenheim, H., and Borchardt, M.: Weitere Beitrag zur Erkennung und Behandlung des Rückenmarks-geschwülste, Deutsche. Ztschr. f. Nervenl. 60:1, 1918.

pital for localized symptoms of disease of the cord, this is the first intramedullary lipoma encountered.

The rarity of this type of lesion was still more strikingly emphasized only a few months ago by Stookey<sup>5</sup> in an article on lipomas of the spinal cord. He was able to find reports of only nine cases in the literature, to which he added one of his own.

A critical review of the cases he reported leads us to feel that the cases reported by Gowers,<sup>6</sup> Turner<sup>7</sup> and Wollbach<sup>8</sup> cannot truly be



# THE BACTERICIDAL PROPERTIES OF THE SOLUTION S.T. 37 (LIQUOR HEXYLRESORCINOLIS 1:1,000) \*

ABBOTT WILLIAM ALLEN, M.D.  
AND  
IRVING SHERWOOD WRIGHT, M.D.  
NEW YORK

This paper is the second<sup>1</sup> in which the results of experiments having a two-fold object are presented. The experiments were made to determine (1) the action of several of the more frequently used antiseptics on some of the more common pathogenic organisms and (2) the reliability of the present standard of evaluating antiseptics as a means of correct appraisal of their practical value. A more detailed report may be expected in a later communication.

In May, 1927, Leonard and Feirer<sup>2</sup> described a new antiseptic known as S.T. 37. It is a practically colorless, odorless, limpid fluid with a warm, sweetish taste, containing 1 mg. of crystalline hexylresorcinol per cubic centimeter of solvent, consisting of 30 per cent glycerin and 70 per cent water. This solution is claimed<sup>3</sup> to be bactericidal to viable bacterial suspensions in fifteen seconds or less. It is further stated to be nontoxic, nonirritating, chemically stable, bactericidal in high dilution, highly penetrating, noncorrosive and nonstaining, and is free from disagreeable odor. Such an antiseptic would be welcomed by the surgeon, especially by the surgeon dealing with traumatic cases, the majority of which come to him in a contaminated condition. Therefore, at the suggestion of Dr. John J. Moorhead, professor of surgery at the New York Post-Graduate Medical School and Hospital, the investigation of this substance was undertaken.

S.T. 37 is an outgrowth of experimentation with resorcinol and allied preparations. The first clinical descriptions<sup>4</sup> of the use of hexylre-

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\* From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.

1. Wright, Irving S.: Effects of Mercurochrome-220 Soluble on the Growth of *Bacillus pyocyaneus*, Arch. Surg. 15:958 (Dec.) 1927.

2. Leonard, Veader, and Feirer, W. A.: Bactericidal Activity of Hexylresorcinol in Glycerine, Bull. Johns Hopkins Hosp. 41:21 (May) 1927.

3. Leonard, Veader, and Feirer, W. A.: (footnote 2): Hexylresorcinol as a General Antiseptic, Surg. Gynec. Obst. 45:603 (Nov.) 1927.

4. Leonard, Veader: Secretion of Bactericidal Urine and the Disinfection of the Urinary Tract, J. A. M. A. 83:2005 (Dec. 20) 1924. Henline, R. B.: Hexylresorcinol in the Treatment of 50 Cases of Infection of the Urinary Tract, J. Urol. 14:119 (Aug.) 1925. Brown, D. A.: Hexylresorcinol in Infection of the Urinary Tract, J. A. M. A. 86:668 (March 6) 1926. Scott, W. J., and Leonard, Veader: Hexylresorcinol in the Treatment of Pyelitis of Infancy and Childhood, Am. J. Dis. Child. 31:241 (Feb.) 1926. Wynne, H. M. N.: Hexylresorcinol in Urinary Tract Infection in Women, Minn. Med. 9:156 (April) 1926. Leonard, Veader: Hexylresorcinol, J. Urol. 12:585 (Oct.) 1924.

Root<sup>12</sup>) the tumors were all pure lipomatous growths. They differ, however, from the case reported here in that they were all apparently infiltrative and not encapsulated.

Stookey discussed at some length the various theories as to the origin of intramedullary lipomatous growths. He does not seem to favor one theory more than another. The fact that in the case here presented the entire tumor was located beneath the arachnoid seems to lend support to the view held by Virchow that it arose from cell rests which became hypertrophic.

The treatment for this type of lesion based on previously reported cases has been against too persistent attempts at removal. As complete enucleation was carried out in this case, we feel that in the future it would be worth while to consider such a procedure in every case. At first inspection in this case the removal of the tumor seemed impossible, but careful manipulation at the sacrifice of a few fibers of the cord finally showed its feasibility. Lipoma is one of the most benign types of lesions, and the removal always holds out a better prognosis for the patient. This, we think, makes it justifiable to do a partial extirpation in all persons with lipoma of the spinal cord when complete removal is not possible.

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13. Root, E. F.: A Case of Lipoma of Spinal Cord, *Utah M. J.*, 1906, 1907, p. 40-42.

is in itself a surface tension reducent. After trying various combinations of the drug, water and glycerin, Leonard and Feirer prepared S.T. 37. This preparation has the lowest surface tension combined with the greatest bactericidal action of any of the many alkylated resorcinol derivatives in varying solvent combinations investigated. Its name signifies a solution the surface tension of which (S.T.) is 37 dynes per centimeter.

Leonard and Feirer used the following protocol<sup>2</sup> to determine the bactericidal efficacy of S.T. 37: Fresh twenty-four hour cultures of the several test organisms were used. A standard 3 mm. loopful of inoculum was introduced into 5 cc. of S.T. 37, from which similar transplants were made to 10 cc. of broth and incubated at 37 C. for twenty-four hours. The transplants were made after fifteen, thirty and sixty seconds, respectively. Suitable controls were made. Failure to obtain growth in the transplants using fifteen different organisms was taken as conclusive evidence that S.T. 37 was bactericidal for those organisms in fifteen seconds or less.

Our preliminary experiments were made with *Bacillus pyocyaneus*, one of the organisms for which S.T. 37 was claimed to be bactericidal in fifteen seconds or less. This work demonstrated to us that the organism of green pus was viable after having been in continuous contact with full strength S.T. 37 for a period in excess of forty-eight hours.

For the detailed experiments to be presented, the organisms used were laboratory stock strains of *Bacillus pyocyaneus* (*Pseudomonas pyocyanea*) and *Staphylococcus aureus*, and a strain of hemolytic streptococcus isolated from the blood of a patient with septicemia following mastoiditis. The cultures before being used were transplanted on agar for five successive days preceding experimentation.

Meat infusion agar slants were used except in the case of *Streptococcus hemolyticus*. For this, the brain agar mediums of Pelouze and Viteri<sup>10</sup> was used, on which the control cultures of the streptococcus grew luxuriantly. The broth was the standard meat infusion dextrose broth. The spinal fluid medium was a mixture of specimens sent to the laboratory for routine examination from patients suffering from meningococcus meningitis or streptococcus meningitis. This fluid was heated at 60 C. Sterility was later proved by absence of growth after forty-eight hours of incubation on agar and in broth. That this medium would support growth was shown by control cultures.

Two different samples of S.T. 37 were used in our work. One was an original 3 ounce bottle; the other was a portion of a similar 12 ounce bottle. Both of these samples were obtained from the Hospital Pharmacy.

With each organism six experiments were performed to ascertain the effect of S.T. 37 under various conditions: (1) undiluted S.T. 37 on a twenty-four hour growth on agar slant; (2) undiluted S.T. 37 applied immediately to a freshly inoculated agar slant; (3) S.T. 37 diluted 1:1 applied to the twenty-four hour growth in spinal fluid; (4) S.T. 37 diluted 1:1 applied to spinal fluid immediately

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10. Pelouze, P. A., and Viteri, L. E.: A New Medium for Gonococcus Culture, J. A. M. A. 86:684 (March 6) 1926.

soreinol in the treatment of the more common types of infections of the urinary tract indicated excellent results. Later reports from other clinicians<sup>2</sup> presented varying degrees of success and failure resulting from its use. In investigating these reports, Leonard, Frobisher and Wood<sup>3</sup> found that certain definite physical factors were involved. They noted that surface tension played a real part in determining the clinical efficacy of the drug. With the ingestion of large amounts of water, sodium bicarbonate or citrates, in conjunction with the hexylresorcinol, a urine of high surface tension and of low bactericidal quality was voided. Reduction of the surface tension of the urine, by preventing the simultaneous use of excessive fluids, bicarbonates and citrates, improved the clinical results obtained with this drug. In fact, the urine itself then possessed a relatively high bactericidal titer<sup>4</sup> following the ingestion of 0.6 Gm. of hexylresorcinol three times daily. This manifestation was attributed to the presence of the drug plus the low surface tension.

In March, 1927, Frobisher<sup>5</sup> demonstrated definitely the effect of surface tension on the action of antiseptics. By lowering or raising the surface tension phase of a solution of phenol, he could appreciably increase or decrease, respectively, the bactericidal potency of the same antiseptic. Within a few months, Leonard and Feiter<sup>6</sup> described the antiseptic which is the subject of this paper.

Hexylresorcinol, per se, has a phenol coefficient of from 44 to 50 according to the United States Public Health Standard, as quoted by Dr. Swenarton.<sup>7</sup> It is readily soluble in glycerin, but sparingly soluble in water. It combines high bactericidal qualities and low toxicity to more than any other similar phenolic preparation. Both of these have a surface tension in excess of 70 dynes per centimeter, while hexylresorcinol

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The results were as follows: All of the controls of the two pathogens were positive, as would be anticipated. None of the streptococcus replants showed any growth, proving the bactericidal effect of S.T. 37 on *Streptococcus hemolyticus* in fifteen minutes or less, whether the antiseptic be full strength or diluted 1:2. However, the replants from the

TABLE 1.—Effect of S. T. 37 on *Bacillus Pyocyaneus*

Organism.....	<i>Bacillus pyocyaneus</i> ( <i>Pseudomonas pyocyanea</i> )					
Medium.....	Agar		Spinal Fluid		Broth	
Dilution of S.T. 37.....	Undiluted		1:1		1:2	
Age of culture.....	24 Hours	1 Minute	24 Hours	1 Minute	24 Hours	1 Minute
Time Interval of Transplants in Hours:						
1.....	+	+	+	+	+	+
2.....	+	+	+	+	+	+
4.....	+	+	+	+	+	+
24.....	+	+	+	+	+	+
48.....	+	+	+	+	+	+

TABLE 2.—Effect of S. T. 37 on *Streptococcus Hemolyticus*

Organism.....	<i>Streptococcus hemolyticus</i>					
Medium.....	Agar		Spinal Fluid		Broth	
Dilution of S.T. 37.....	Undiluted		1:1		1:2	
Age of culture.....	24 Hours	1 Minute	24 Hours	1 Minute	24 Hours	1 Minute
Time Interval of Transplants in Minutes:						
15.....	0	0	0	0	0	0
30.....	0	0	0	0	0	0
90.....	0	0	0	0	0	0
150.....	0	0	0	0	0	0

TABLE 3.—Effect of S. T. 37 on *Staphylococcus Aureus*

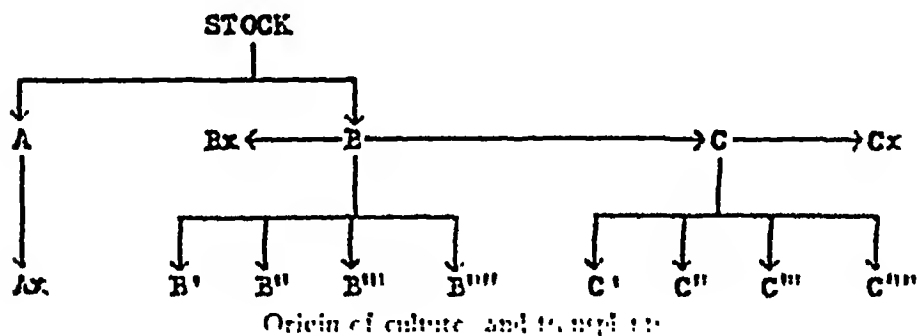
Organism.....	<i>Staphylococcus aureus</i>					
Medium.....	Agar		Spinal Fluid		Broth	
Dilution of S.T. 37.....	Undiluted		1:1		1:2	
Age of culture.....	24 Hours	1 Minute	24 Hours	1 Minute	24 Hours	1 Minute
Time Interval of Transplants in Minutes:						
15.....	+	0	+	0	+	0
30.....	0	0	0	0	0	0
90.....	0	0	0	0	0	0
150.....	0	0	0	0	0	0

twenty-four hour growth of *Staphylococcus aureus* were positive in the fifteen-minute tubes of all three mediums, and positive as well in the broth replant at the end of the thirty-minute period (table 3). None of the fresh (C tubes) of *Staphylococcus aureus* replants showed any growth. Hence, S.T. 37 is bactericidal to *Staphylococcus* in either concentrated form or diluted 1:2 in some time under ninety minutes.

after inoculation: (5) S.T. 37 diluted 1:2 applied to *Cx* twenty-four hours after in broth; (6) S.T. 37 diluted 1:2 applied immediately to the freshly inoculated broth culture.

For each organism the following procedure was used, except as specially noted. From the fifth daily successive transplant, two tubes were incubated and fixed at 37 C. for twenty-four hours. The next day, tube *Ax* was planted from *A* to prove the viability of *A*; these two were subsequently used as comparative controls of growth. From tube *B*, two new transplants were made: *Bx*, a transplant from *B* to prove the viability of *B*, and tube *C*, which was a fresh incubation. As soon as it was possible after inoculating *C*, *Cx* was incubated as a control of *C*, being planted on agar. S.T. 37 was immediately added to both *B* and *C* tubes, the whole procedure requiring approximately one minute between the time of inoculating *C* and adding to it the antiseptic. Tubes *A*, *Ax*, *Bx* and *Cx* were incubated at 37 C. for twenty-four hours, and served as controls.

Experiments *B* and *C* were further conducted as indicated in the accompanying figure. At the end of intervals, measuring from time of addition of the S.T. 37, one loopful of the fluid culture medium with its recent admixture of antiseptic was streaked on an agar slant and recorded with the time as *B'*, *B''*, or *B'''*, *C'*, *C''*, or *C'''*, etc.





# THE FUNCTION OF THE DIAPHRAGM\*

WILLIS S. LEMON, M.D.

ROCHESTER, MINN.

The relationship between the action of the diaphragm and the intercostal muscles, as well as the muscles of less importance, in making respiration possible by rhythmically enlarging and decreasing the volume of the thoracic cavity has been the subject of discussion by clinicians, surgeons and physiologists. Many valuable observations have been made which, at the present time, form a background for further observation and a fund of information from which to draw, as need arises, during the progress of research. In time, certain fixed opinions become accepted as facts, often because they are stated with emphasis, owing to the conviction of their authors. As truth is relative and corresponds with the best thought of a period, these opinions are true unless they can be proved incorrect, inaccurate or incomplete.

For one to replace an old truth by a wider and more accurate conception of fact requires that the observer make use of all available information and therefore include a survey of the embryologic, anatomic, physiologic and clinical knowledge of others as well as his own. In this survey the action and purpose of the diaphragm as a respiratory organ will be considered from these several points of view, from each of which, it is believed, valuable implications will be discovered.

## EMBRYOLOGY

Prentis and Arey, Ballantyne, Keibel, Hume and Mall agree that the development of the diaphragm is a complex and obscure part of organogenesis, and that it is derived from sources other than the septum transversum in which His recognized its anlage, the most important being the pericardiopleural and the pleuroperitoneal membranes. All observers agree that the beginning of the diaphragm is in the early development of the embryo (the third week of which is so picturesquely described by Ballantyne), that its origin is high toward the head and that it migrates caudally and occupies different planes as it passes into the celom to become one of the most important structures which divide it into its several compartments.

Thus, the first chief partition has been the anlage of the diaphragm recognized by His in a mass of mesoblastic tissue situated, with the

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\* From the Division of Medicine, The Mayo Clinic.

In a previous paper, one of us (I. S. W.)<sup>2</sup> showed that nutrient-chrome-220 soluble is ineffective as a germicide against *Bacillus pyocyaneus*, while tincture of iodine killed the same organism under exactly the same conditions. The number of antiseptics and other bactericidal preparations is well known to the medical profession. Many have been proposed with a statement of their phenol coefficient, and from this, with or without sufficient experimental proof, their respective bactericidal properties have been claimed. As one reviews the literature of antiseptics and as one notes the actual efficacy of antiseptics, one is led to question the value of the phenol coefficient as a standard for the proper evaluation of modern antiseptics for practical use.

#### CONCLUSIONS

1. S.T. 37 is not effectively bactericidal for *Bacillus pyocyaneus* in forty-eight hours or less.
2. S.T. 37 is bactericidal for *Staphylococcus aureus* in some time under ninety minutes.
3. S.T. 37 destroys *Streptococcus hemolyticus* in less than fifteen minutes.
4. S.T. 37 is stable and active in spinal fluid.

elasmobranches, this septum is not complete, failing to reach the other (splanchnic) wall, thus leaving one or more openings, pericardioperitoneal canals, connecting the pericardium with the body. In the higher vertebrates, the closure is complete.

In all the lung-bearing vertebrates except the mammals, the lungs are suspended in the general body cavity (splanchnoceles), but in the latter group a second partition, the diaphragm, cuts off a pair of pleural cavities from the rest of the splanchnocoele which is now called the peritoneal cavity.

Traces of structures similar to the diaphragm as indicated by nerve supply, and so forth, occur in vertebrates as low as the amphibia, but their exact homology is uncertain.

*Comparative Anatomy of Vertebrates.*—Discussing the derivation of the muscular tissue of the diaphragm, Kingsley said: "The diaphragm undergoes several shiftings of position before reaching its final place. The dorsal part of the diaphragmatic muscles is derived from the original folds, the ventral comes from the rectus abdominis muscle of the ventral abdominal wall." This makes a concrete addition to Broman's fifth division and will be referred to when the effect of phrenic neurectomy is discussed.

The study of the development of the diaphragm at different periods of fetal life introduces implications that suggest anatomic and functional probabilities. Yet there is an old method of study that may promise better results, and it is based on the obvious and well recognized fact that in the development of animal life the necessity for expanding function requires a development of organic machinery that makes function possible. This philosophy has been advanced most convincingly by Jones in his description of diaphragmatic derivations and function. It is therefore clear that when new activities and functions are contemporaneous with a new organ, the latter should be considered as responsible for the operation of the former. But functions have a tendency to develop slowly, and nature develops organs, at first simple in design and then more complex, until perfection of function is brought about by perfection in detail of the organ. Thus three pictures must be considered. When the necessity for development and for physical activities required a more efficient means of bringing oxygen to the tissue cells, the superficial layers folded in, and the first hint of a future lung was apparent. These first infoldings multiplied in number, the original lymph system became a hemolymph system, and the relationship between the circulation and respiration became established. Then the organism developed the ability rhythmically to enlarge and decrease the size of its body cavity and to produce within itself a negative pressure. Air-breathing lungs appeared and, bridging the many intermediate variables in form and design, a second picture can be visualized.

In such an animal the machinery for respiration is adequate to the needs of the animal's activities. It has lungs lying in a single celomic



*Anatomy in Man.*—The anatomy of the diaphragm in man as well as in all mammals is so familiar as not to require detailed description. It is, however, important to review the opinion of anatomists and later to appraise these opinions in the light of more recent experimental evidence. LeWold has anticipated this discussion by calling attention to the fact that the diaphragm is not essential to active life in animals below the mammals. He cited the endurance and strength of the ostrich as an example of the activity possible in the absence of a diaphragm, and comparative anatomists agree that animals below the vertebrates do not have a semblance of a diaphragm, and none below the mammals has a perfected partition. Anatomically, then, the diaphragm serves as a partition dividing the celom into its two chief chambers; it belongs to those groups of muscles which serve to enlarge and decrease the volume of the chest and which are thus important in a mechanical way for respiration. This set of muscles can be seen in action to cooperate with other groups and to act in coordination with them, and its share consists in enlarging the long diameter of the cavity of the chest. The statement found in the older textbooks on anatomy as well as in those of more recent date, that the diaphragm, next to the heart, is the most essential muscle of the body and again that it is the most important muscle of respiration, requires sober thought and perhaps modification.

#### ACTION OF THE DIAPHRAGM

When at rest, the diaphragm presents a domed surface due partly to the positive intra-abdominal pressure and partly to the negative intrapleural pressure. It rises higher in the thorax on the right side than on the left. During inspiration it moves downward, producing pressure on the abdominal viscera and distending the abdomen. At the same time the margins of the ribs pass outward and upward. Although the central portion moves least, the right to a greater extent, and the left through the greatest excursion, the combined movement produces an increase in the vertical diameter of the chest, and inspiration of air occurs. Although the abdominal increase in pressure during the descent of the diaphragm tends to distend the abdomen, yet, because there is opposition, the central tendon becomes a fixed point and the circumferential muscles in contraction actually elevate the lower ribs and expand the lower part of the thoracic cavity. In all acts of expulsion, sneezing, coughing, laughing, vomiting and crying, for example, the diaphragm adds power to expulsive effort.

Such was the opinion a generation ago. More recently Cunningham said: "The diaphragm, after the heart, is the most important muscle of the body. It forms the dome-shaped roof of the abdomen and the highly convex floor of the thorax." The first sentence states a belief in functional importance, the second is purely a statement of anatomic



increases the subcostal angle by increasing the intra-abdominal pressure. This pressure exerted on the abdominal contents, which are comparable with a fluid, becomes hydrostatic in character and is transmitted equally in all directions, forcing outward not only the abdominal wall but the margins of the ribs.

One other function needs discussion, the effect of diaphragmatic contraction on the blood pressure. Because of the increase in the intra-abdominal pressure the viscera are crowded against the inferior vena cava, blood is forced into the thorax and the immediate effect is that of raising the blood pressure temporarily. Before inspiration is complete the lessened flow tends to decrease the blood pressure. Abdominal respiration produces an initial rise succeeded by a fall in blood pressure during inspiration and an initial fall followed by a rise in pressure during expiration. These results are opposed by the effect on pressure caused by thoracic breathing in which the pressure falls and later rises during inspiration. The effect of combined breathing is the algebraic sum of these opposing influences.

Before the experimental phases of the subject are discussed, it is necessary to revert here to the sentence: "The diaphragm, after the heart, is the most important muscle of the body." I shall offer substantiation of the statement because otherwise the experimental work would lend color to the belief that the sentence is an overstatement of fact. The work best designed to influence judgment was done by Guenther and Meleney, who showed the contrast between the periodic and irregular contractions of skeletal muscles and the regular rhythmic movement of the diaphragm which is comparable with that of the heart. Like the heart muscle, the diaphragm enjoys only a brief period of rest between contractions, and the rest periods are approximately equal in length. The same remarks apply also to the other muscles regularly employed in producing inspiration and expiration. The comparison of the physiologic properties of the diaphragm with those of the extensor longus digitorum, the sartorius and the soleus convinced these authors that the diaphragm had the most efficient muscle tissue.

The diaphragm offers certain points of analogy to the muscle of the heart and in that sense partly justifies Cunningham's belief in its importance. Circulation and respiration are both fundamental and equally essential functions of the body; both are produced by muscular action, the latter only partially dependent on the diaphragm and capable of continuance without its action, the former absolutely dependent on the contraction of the heart. It may be that the diaphragm is second only in importance to the muscle of the heart but because respiration and circulation are equally essential to life, the muscular function which is dispensable suffers by comparison with that which is indispensable.





lowered vital capacity and slowed the venous stream within the abdominal veins. My impression is, however, that the abolition of the resistance of the abdominal musculature against the downward thrust of the diaphragm has more to do with postoperative conditions than has been supposed. There are other considerations. The dog does not lie on his back; he is not trussed up with dressings, adhesive bandages and encircling binders that compress the margins of the ribs and prevent movement at the bases of the lungs where movement is most necessary to prevent congestion. With a slowed venous stream and a congested lung, both infarct and infection become not only possible but even probable. The low vital capacity in man is more an expression of abdominal pain preventing resistance to diaphragmatic contraction than to any loss of power in the efficiency of the diaphragm itself.

#### UNILATERAL PHRENIC NEURECTOMY

When evulsion of the phrenic nerve is carried out, half of the diaphragm is promptly paralyzed. Atrophy starts as early as the second day, and is manifested grossly by pallor and edema in both dog and man. The diaphragm rises in the thorax and does not take any further part in respiration. It either is immobile or takes on paradoxical movement due to the alteration in intra-abdominal pressure that is produced by contraction of the unaffected portion. The only difference between the dog and man lies in the higher elevation of the vault of the paralyzed hemidiaphragm in man. I have noticed this in examining all of my animals and comparing them with the human subjects on whom unilateral phrenicotomy had been performed for various reasons, as well as those rather rare cases of true eventration of the diaphragm. It has seemed to me that the cause was to be found in the difference between the pronograde and the orthograde animal and in the purely carnivorous and the partly carnivorous types. The relatively small abdominal content in the carnivorous group fails to elevate the paralyzed portion to the same degree.

The movements of the thoracic wall have been studied both in animals and in man. Kymographic records have been made to check inspection, but in every instance the movements of the chest as a whole and of its several parts have remained unchanged. It was expected that the movement of the costal margin would be increased on the side affected, but this could not be substantiated in my experiments. I have been unable to convince myself by any means at my disposal that such a phenomenon is present in man, and I have examined patients repeatedly for days after phrenic neurectomy, patients with eventration and a single patient who was shown at operation to have congenital absence of half of the diaphragm. Lord, in discussing cases

## EXPERIMENTAL AND CLINICAL OBSERVATIONS

Because of the growing popularity of phrenic neurectomy in the treatment of both tuberculous and suppurative pulmonary disease, it became necessary to study the effect of such an operation on normal subjects. Study of the physiologic effect in general, as well as the respiratory mechanism, was undertaken. Healthy dogs were used in all the experiments. Later I became aware that similar work had been done on horses. Results of the study of the physiology in man could not be conclusive except in rare instances because the operation was not indicated except in cases in which the extent of involvement made it impossible to separate pathologic change from physiologic change due to the operation with consequent loss of function of at least half of the diaphragm. Suitable cases, however, have been under observation and will be discussed as they apply to the various divisions of the experimental work.

The effect of abdominal incisions and of major surgical operations on the upper part of the abdomen was studied first, because of the belief that such operation caused fixation of the diaphragm and contributed to the prevalence of postoperative pulmonary complications, which are known to be relatively much more common in cases in which the patients have been treated surgically for conditions of the stomach and gallbladder than in general surgical work. The experiments were carried out in several stages. Observations were made in the various cases studied: (1) when a simple incision in the skin constituted the surgical intervention; (2) when the abdominal wall was cut through and the abdominal cavity opened; (3) when an Eck fistula operation was performed; and (4) when an Eck fistula operation was performed and various fractions of the liver were removed. The animals were examined clinically and fluoroscopically immediately after the operation, when the animal first became conscious and every succeeding day until the wound was healed. In none of the animals was any fixation of the diaphragm discovered. The excursion was normal and equal to that before operation. I have never seen an animal under any of these conditions with restriction of diaphragmatic movement.

This observation is not reported in an iconoclastic spirit. It has to do with an animal and not with man. I do not know whether it is a true statement in regard to the diaphragmatic movement in man under similar circumstances. No one, to my knowledge, has made any such experimental study on man. The reports have been based on purely clinical examination and are therefore subject to personal error. No one can reproduce in a dog the conditions found in man: the debility that called for the necessity of operation, the anxiety and apprehension before and after operation, and the acuteness of sensibility to pain that

was reduction in vital capacity of approximately 20 per cent, but within nine days the capacity reading was normal. In another case, left phrenic neurectomy was done because of localized bronchiectasis, and symptomatic cure resulted. The patient does her housework without respiratory embarrassment, and she is not troubled with dyspnea or gastric distress. Cough is infrequent, and more effectual in raising sputum than before operation. The vital capacity reading is 3,403 cc. The estimated normal reading would be 3,050 cc. The removal of 8 cm. of the phrenic nerve paralyzed the left side of the diaphragm, which rose high in the thorax and was immobile on both general and fluoroscopic examination. The left side of the chest measured 38.5 cm. and the right 39 cm., a difference so small that it may be explained as a personal error or may represent what could be called normal asymmetry of the chest. Differences in the movement of the chest could not be observed by inspection, by combined inspection and palpation or by actual measurement during inspiration or when at rest. These observations were checked by observers who were not acquainted with the patient's history and were entirely disinterested and unprejudiced.

Three other patients were dyspneic on exertion, but other complications were present that may have been responsible for the dyspnea. Welles did not observe any evidence of undue shortness of breath or any abdominal disturbances after the operation in forty-nine of fifty cases of unilateral phrenicotomy. Yeates performed eighteen radical operations of extraction or resection and reported that none of the intra-abdominal functional disturbances could be attributed to the paralysis. "Paralysis of the diaphragm reduces vital capacity, restricts external respiration and impairs competence. Dyspnea on exertion is inevitable." Experimental evidence permits certain definite conclusions: 1. A dog can live comfortably without diaphragmatic movement. 2. He can live for many days following transection of the spinal cord between the sixth and seventh cervical vertebrae so that the diaphragm is almost totally responsible for respiration. 3. He can still live even after transection of the cord and evulsion of one phrenic nerve.

Conversely, clinical evidence permits the conclusion that a man can live after a low fracture of the neck has paralyzed thoracic and abdominal muscles and the diaphragm is almost entirely responsible for respiration. I have examined three such patients living almost entirely from diaphragmatic movement. The chest as a whole retracted with inspiration and the consequent increased negativity of intrapleural pressure, but the costal arches and margins moved outward because of the increased positive pressure due to the descent of the contracting diaphragm.

It was formerly said that man, unlike a dog, cannot live if he loses diaphragmatic function. I have not examined a case in which there was



# THE SURGICAL SIGNIFICANCE OF THE ABDOMINAL REFLEXES \*

WILLIAM KLEIN, M.D.

NEW YORK

The diagnosis of acute intra-abdominal diseases has taxed the ability of the internist, pediatrician and surgeon alike. The literature on the subject is voluminous, but most writers have not stressed the signs which do not require the assistance of the laboratory. Any symptom that can be elicited at the bedside is a welcome aid to the diagnostic armamentarium.

The cutaneous abdominal reflexes have not received their proper place as a valuable aid in the diagnosis of acute intra-abdominal disease. The literature on this topic is scant. Most writers have dealt with hyperesthesia, but the contraction reflex has been singularly omitted. Smith <sup>1</sup> is an outstanding exception. The neurologists, such as Monrad-Krohn <sup>2</sup> and others, spoke of abdominal reflexes and did not include hyperesthesia, whereas, surgeons, such as Robinson, <sup>3</sup> Logat <sup>4</sup> and Cope, <sup>5</sup> captioned their articles abdominal reflexes and described hyperesthesia of the skin, but failed to mention the contraction reflex. Both are important and may be significant in the same pathologic condition. It is essential, therefore, to bear in mind that hyperesthesia and the contraction reflex are not the same.

Hyperesthesia may be defined as a response to a stimulus expressed in terms of pain. It is, in reality, a form of hyperalgesia, as is all abdominal tenderness due to visceral inflammation. Its interpretation is dependent on the patient's statement and cooperation. It becomes evident that this reflex pain cannot be controlled by the patient. It is not definitely known how this increased pain over an inflamed abdominal organ is produced. Livingston <sup>6</sup> believed that it is caused by the transmission of the painful sensation by the visceral nerves through the nervi communicanti to the spinal nerves and so to the overlying skin.

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\* Read before the Bronx Surgical Society, April 25, 1928.

1. Smith, R. R.: Surg. Gynec. Obst. Oct., 1914, vol. 19.

2. Monrad-Krohn, G. H.: Norsk Mag. f. Lægevidensk., Dec., 1918, suppl. vol. 79.

3. Robinson, H.: Quart. J. Med. 1:387, 1908.

4. Logat, D.: Lancet 1:724, 1919.

5. Cope, Z.: The Early Diagnosis of the Acute Abdomen, New York, Oxford University Press, 1924.

6. Livingston, E. M.: Further Study of Viscero-Sensory Phenomenon, J. A. M. A. 82:1495 (May 10) 1924.

bilateral phrenic paralysis. Jones said that the primitive (pronograde) mammal is dependent on the external respiratory system, while man has become dependent on the internal respiratory system. He believed this dependency to be due to the loss of fixation of the fore limb and shoulder girdle. This hypothesis, however, is no longer accepted. It is well known that man can live not only with half of the diaphragm paralyzed, but also with the whole diaphragm rendered functionless. Cases reported by Gamble, Pepper and Mueller and also by Dowman confirm this belief.

#### EXPERIMENTS ON ASPIRATION

Because of the importance of aspiration of secretions into deep portions of the bronchial tree, thereby adding to the total amount of infected lung, it became necessary to determine whether there was sufficient suction during inspiration to cause such aspiration in an animal the hemidiaphragm of which is paralyzed. This is an important consideration in both tuberculous and chronic suppurative conditions in both of which infection may be spread by aspiration. Accordingly, an animal with half of the diaphragm completely paralyzed was anesthetized with ether for twenty minutes during which time 40 per cent iodized oil was slowly introduced into the trachea. Ten minutes later he was killed by overetherization, the trachea being clamped to maintain expansion of the lungs. The lungs were examined fluoroscopically and oil was seen to have been aspirated into both lungs, showing that the paralyzed diaphragm did not affect inspiratory suction sufficiently to prevent the aspiration of intratracheal material. One cannot hope that in such diseases as tuberculosis and bronchiectasis the lungs will be spared from the risk of aspiration.

#### NECROPSY REPORT

The examination of dogs at necropsy did not show evidence of abnormality in the heart, pericardium, pleura or lungs. Evidence was lacking of congestion or other impairment in the circulation of blood through the lungs. Brown's later work confirmed the conclusions reached from my gross and microscopic data, although his method of study was entirely different. My own observations have been repeated many times, and the conclusions have remained unchanged. Thus far I have not been able to produce evidence that the diaphragm has a double motor innervation, although the embryologic development might lead one to suspect that nerves supplying the muscles of the body wall might also supply that portion of the diaphragm which is derived from them. Higgins has discovered that the thirteenth thoracic nerve in the dog sends fibers to the diaphragm, but there is no assurance that this is motor in function.

must be remembered that pain is a relative term, and can be interpreted only by comparing both sides of a particular segment. It is of much value in the adult, but cannot be relied on in children, as the young will mislead when asked which side is more sensitive. This capacity for hyperesthesia in disease persists till late in life, and can be extremely active from adolescence till about 50 years of age. From then on it diminishes, and it is of little value in old people. This reflex is present early in the pathologic process. When the inflammation progresses and the peritoneum becomes involved, it diminishes in intensity and is finally lost in the late stages of peritonitis. At this stage, the contraction reflex is of value, as will be shown later.

The cutaneous contraction reflex is produced by scratching the skin with a sharp, pointed object, such as a pin or a sharp pencil. It is seen as a homolateral, segmental contraction of the muscular segment at the site of stimulation. The linea alba and the umbilicus deviate to the same side. This contraction occurs almost simultaneously. A heterolateral contraction is pathologic and usually belongs to diseases of the spinal cord, such as poliomyelitis.

After the first six months of life, this reflex is extremely active and can be elicited in the young. It persists actively in the young and diminishes in importance in the older person. The retrogression is not alike in both sexes. It persists longer in the male and is at times seen late in life. In the female, it tends to diminish with the advance of adiposity and the relaxation of the abdominal wall consequent on child bearing. These patients retain part of their contraction reflex in the upper part of the abdominal muscles which overlie the lower costal cartilages; here the amount of fat is scant, and the striae due to stretching of the muscles are absent. It is interesting to note that the abdominal wall of obese males retains the contraction reflex longer than a similar abdominal wall in the female.

From the foregoing considerations, it becomes evident that the hyperesthesia is of value in the adult while the contraction reflex is of inestimable value in children.

For convenience, the abdominal wall may be divided into four parts: upper right and left and lower right and left. Some neurologists speak of gastric, umbilical and midabdominal areas, but for the practical purposes of the surgeon, the division into four parts is sufficient.

In eliciting the contraction reflex, the pointed instrument should be almost perpendicular to the skin. In the upper segments of the abdomen, the motion should be from above downward. Beginning at about the tenth costal cartilage just lateral to the nipple line, the stroke is directed downward for about 8 cm. In the lower parts the scratch is lateral, beginning away from the median line and directed inward. The linea alba must not be crossed.

The cutaneous contraction reflex can be defined as a response to a stimulus expressed in terms of involuntary muscular contraction, usually not accompanied by pain. Here the element of correct interpretation is independent of the patient's statement or intelligent cooperation. It is, therefore, of inestimable value in children.

The paths and mechanism of this contraction reflex is not definitely known. Many neurologists believe that they are cerebral, while others think that the complete cycle is in the spinal cord. Whether one or the other view is correct, it seems to me that other factors enter into its mode of production and repression.

The anterior abdominal wall is supplied by the lower seven intercostal nerves, which carry the motor and sensory fibers. The muscles of the abdominal wall are of the voluntary group and can be contracted and relaxed at will. Normally, one either contracts or relaxes the whole anterior abdominal wall, but does not have control over any particular segment. The cutaneous reflexes, whether hyperesthesia or muscular contraction, differ in that they are unilateral and segmental. The hyperalgesia cannot be controlled by the patient, that is, the pain is present whether the patient says so or not. The contraction reflex can be controlled by voluntarily holding the muscles in a state of tension. Experimentally, it was shown that when the cutaneous nerves are severed, the muscular tone is still maintained, but the reflexes are abolished. The fact that the voluntary control of the abdominal muscles is synchronous on both sides while the normal reflexes are unilateral and segmental is more evidence that the muscular control and the cutaneous reflexes have different centers. It therefore seems logical to conclude that the cutaneous reflexes are spinal, but that the muscular control is elsewhere, probably in the cerebral system. As will be shown later, there may be rigidity of the abdominal muscles with the reflexes exaggerated, diminished or absent, depending on the underlying cause of the rigidity.

#### GENERAL CONSIDERATIONS

The cutaneous abdominal reflexes are absent in the first six months of extra-uterine life. They become active in the second half of the first year, and their presence at this age can be elicited with difficulty. From then on they differ in their activity and are not to be interpreted in the same way.

Hyperesthesia consists of a sensation of increased pain when the skin over a particular area is pinched. Only the skin must be stimulated, and not the underlying tissues. It is present in the early stages of disease of an intra-abdominal organ. The pathologic condition must not necessarily be an acute inflammation. Any process that causes increased tension, increased peristalsis or acute inflammation will give hyperalgesia. It



When the reflexes are absent early, the condition is indicative of a marked peritoneal involvement, and immediate interference is imperative. The following case illustrates this fact.

CASE 2.—M. Scoglio, a girl, aged 11 years, had been operated on by me for an acute appendicitis on Feb. 2, 1928. The abdomen was drained for a few days. At that time, I noticed that the gallbladder was much enlarged. In the presence of infection, I refrained from doing anything to this organ. The patient was discharged on February 19, cured. On March 11, she began to complain of pain in the abdomen, mostly on the right side. Vomiting began soon afterward and continued for eight hours. When I saw her in consultation with Dr. Astrachan, the temperature was 101 F., the pulse rate 98 and the respirations 26. The abdomen was distended and extremely tender throughout. The abdominal reflexes were absent. In view of the previous laparotomy, a tentative diagnosis of intestinal obstruction was made. As the reflexes were absent, peritonitis was thought of, but was mentioned only as a probability. On making an incision into the abdomen, I found a ruptured gallbladder. This well illustrated that the absence of the reflexes was too early for an intestinal obstruction, but indicated peritonitis.

In cases of fulminating peritonitis, such as pneumococcus or streptococcus forms, the reflexes are absent early and throughout the entire abdominal wall. In hemic peritonitis, the contraction reflexes are present at first, but tend to diminish later as absorption from the peritoneal cavity takes place. This is of some significance in children but not in adults. In cases of rupture in ectopic pregnancy, it is generally of less value as these patients are often obese and frequently multiparae.

Cases of ruptured appendixes occur in which the contraction reflex is only diminished. In these, the appendix is retrocecal, and the toxic material has not invaded the anterior parietal peritoneum. The process, however, soon extends and the anterior wall becomes involved. The reflexes are then abolished.

It must not be concluded that all forms of abdominal rigidity show an absence of this reflex. When the rigidity is the result of a general involvement of the nervous system, as for instance, meningitis, the abdomen may be rigid and the reflexes markedly exaggerated. This is well illustrated in the following case:

CASE 3.—H. M., aged 22, a drug clerk, while carrying a ladder, had felt a severe pain over the abdominal wall. It soon radiated to the back and was followed by a mild chill. Two hours later, he vomited twice, and the pain in the abdomen increased. Two enemas were ineffectual. I saw him twelve hours later. Examination revealed a rigid abdomen, with tenderness more marked on the right side. The patient could not retain anything taken by mouth and appeared ill; the temperature was 101 F., the pulse rate 90 and the respirations 26. The contraction reflexes were exaggerated, and the spine was somewhat rigid. The condition proved to be meningitis. The exaggerated reflexes drew my attention to the spine. I confess that if it had not been for the reflex phenomenon, this patient might have undergone a laparotomy.

The cremasteric reflex cannot properly be called an abdominal reflex, as the cremasteric muscle is supplied by the external spermatic branch of the genitofemoral nerve. This reflex can be elicited in the triangle formed by a line drawn from the middle of Poupart's ligament inward and meeting the sartorius muscle which forms the inner boundary of the triangle. This reflex is exaggerated in cases of ureteral colic or other diseases of the urinary tract and remains unaffected by intra-abdominal pathologic changes. It is, therefore, of great help in distinguishing ureteral colic from acute appendicitis.

I have studied 200 cases with relation to these reflexes. Special attention was paid to the contraction reflex as this, to my mind, is the more important of the two. Besides, the hyperesthesia reflex is present in only about 50 per cent of the acute cases in adults, in which cases the diagnosis is not as difficult.

As a general statement, it can be said that whenever the anterior parietal peritoneum becomes involved in an acute inflammatory process, the cutaneous contraction reflexes are abolished. The degree of suppression is in direct ratio to the severity of the pathologic process. The area of absence of this reflex overlies the diseased organ. When the peritonitis is diffuse; the whole abdominal wall is nonresponsive. In well localized inflammatory processes, such as appendicitis and pericholecystitis and others, the overlying area of skin does not respond to the scratch. The immediately surrounding areas show a diminution of this reflex and the opposite side responds normally.

In children, in whom it is often difficult to differentiate between intrathoracic lesions and an acute surgical condition of the abdomen, I find that in the former condition the abdominal contraction reflex is present and exaggerated while in the latter this reflex is abolished. This is well illustrated in the following case.

#### REPORT OF CASES

CASE 1.—J. Lubell, aged 4 years, had a past history that was irrelevant. The child began to complain of pain in the abdomen at 7 p. m.; he vomited soon afterward. This pain continued intermittently all night. I saw the child with Dr. Blutstein at about 10 a. m.; at this examination, the child looked ill. The temperature was 103 F. and the abdomen was tense, but a satisfactory examination could not be made as the child cried continually. Repeated enemas since the previous night were not of avail. Examination of the chest did not reveal any definite signs of a pulmonary lesion. The abdomen was distended, and the contraction reflexes were somewhat exaggerated; this ruled out peritonitis. The diagnosis of pneumonia was confirmed thirty-six hours later. The child recovered.

In cases of intussusception or other forms of intestinal obstruction, the contraction reflexes are present at first but diminish later. When gangrene sets in or the transudate becomes toxic, the reflex is abolished.

# RELATION OF BACILLUS WELCHII ANTITOXIN TO THE TOXEMIA OF INTESTINAL OBSTRUCTION

## EXPERIMENTAL STUDIES \*

JOHN J. MORTON, M.D.  
AND  
SAMUEL J. STABINS, M.D.  
ROCHESTER, N. Y.

It is now generally recognized that death in cases of intestinal obstruction is due to the establishment of a toxemia. Two main theories have been advocated to account for the formation of the toxin concerned. One group of investigators<sup>1</sup> believes that the toxin is elaborated by a perversion of function of the mucosa cells lining the obstructed loop; the other group<sup>2</sup> assumes that the bacterial flora within the loop is responsible. The weight of experimental evidence to date is difficult to evaluate, but a communication by Williams<sup>3</sup> demands that we investigate a known bacterial toxin which may possibly have a bearing on the problem. Williams thinks that the toxemia results from the absorption of *Bacillus welchii* toxin. He gives evidence of the proliferation of the organism in the small bowel in cases of obstruction, and likewise of the presence of the toxin by the injection of the loop filtrate into mice; however, he has been unable to show that this toxin is absorbed. In a recent publication, Scholefield<sup>4</sup> concludes that the toxemia is due to the absorption of a toxin through the portal circulation.

## EXPERIMENTAL WORK

The following experiments were undertaken to test the validity of Williams' observations. A standard experiment was used throughout, the conditions being maintained as nearly constant as possible. In dogs that were not fed the day

\* From the Department of Surgery, University of Rochester School of Medicine and Dentistry.

1. Whipple, G. H.; Stone, H. B., and Bernheim, B. M.: Experimental Studies in Intestinal Obstruction, *J. Exper. Med.* **17**:286, 1913; *Am. Surg.* **59**:714, 1914. Whipple, G. H.; Rodenbaugh, F. H., and Kilgore, A. R.: Intestinal Obstruction, Proteose Intoxication, *J. Exper. Med.* **23**:123 and 135, 1916.

2. Murphy, F. T., and Vincent, Beth: The Cause of Death in Intestinal Obstruction, *Boston M. & S. J.* **165**:684, 1911. Murphy, F. T., and Brooks, B.: Intestinal Obstruction, *Arch. Int. Med.* **15**:392 (March) 1915. Dragstedt, L. R.; Moorhead, J. J., and Bureky, F. W.: Intoxication of Closed Intestinal Loops, *J. Exper. Med.* **25**:421, 1917. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Extirpation of the Duodenum, *Am. J. Physiol.* **46**:584, 1918. Dragstedt, C. A., Cannon, P. R., and Dragstedt, L. R.: Effect of Acute Obstruction and Stasis on Bacterial Types, *J. Infect. Dis.* **31**:209, 1922.

3. Williams, B. W.: Toxemia of Intestinal Obstruction, *Brit. J. Surg.* **14**:295, 1926.

4. Schoelfield, B. G.: Acute Intestinal Obstruction, *Guy's Hosp. Rep.* **77**:160, 1927.

## CONCLUSIONS

1. The cutaneous abdominal responses are of two kinds: (1) hyperesthesia, which is increased pain when the skin is pinched over a diseased organ, and (2) the contraction reflex, which is a response to scratching of the skin over a particular area.

2. Hyperesthesia is of value in diagnosing conditions in adults, while the contraction reflex is helpful in diagnosing disease in young persons.

3. Hyperesthesia is present early in the course of abdominal disease (in about 50 per cent only) and diminishes later. The contraction reflexes are absent when the peritoneum becomes involved.

4. Both reflexes are unilateral and segmental.

5. Rigidity of the abdominal wall, not the result of an intra-abdominal condition, may be accompanied by an exaggerated contraction reflex, while that caused by inflammation of the peritoneum results in the absence of this reflex.

6. In the obese and multiparas, the absence of the contraction reflexes is not of any particular significance, but the hyperesthesia has definite value.

essentials from that observed by other investigators. It corresponds well with Haden and Orr's control series.<sup>6</sup> Most of the animals died in from three to four days with a rapid rise in nonprotein nitrogen. Occasionally, an animal failed to develop toxemia and the blood chemistry remained practically normal for over a week (dogs 2 and 3). The case of dog 3 is especially interesting in that the nonprotein nitrogen started at a high level and remained there for so long a time without toxic symptoms. The kidneys of this animal, however, showed chronic nephritis, which probably accounted for the observations.

TABLE 1.—*Obstruction of the Jejunum in Untreated Dogs*

Dog No.	Day after Operation	Blood, Amount per 100 Cc.		Comment
		Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	
1	0	30.0	531	Obstruction
	1	40.7	435	
	2	40.2	456	
	3	45.8	386	
	4	66.6	315	
2	0	23.1	531	Obstruction
	1	28.2	498	
	2	23.0	473	
	3	33.5	503	
	4	23.8	461	
	5	20.8	468	
	6	27.1	444	
	7	25.5	465	
	8	30.4	405	
	9	26.0	423	
3	10	63.0	421	Died
	0	40.0	508	
	1	37.5	498	
	2	68.4	360	
	3	71.5	335	
	4	80.0	316	
	5	76.9	286	
	6	83.0	312	
	7	75.0	321	
4	8	82.2	260	Obstruction
	0	33.3	515	
	1	30.8	457	
	2	31.5	396	
	3	32.6	373	
5	4	68.2	...	Died
	0	23.4	490	
	1	31.6	433	
	2	33.3	422	
	3	28.6	398	
	4	30.8	397	
6	5	44.8	...	Obstruction
	0	33.1	522	
	1	23.8	428	
	2	31.6	386	
	3	35.5	390	
	4	67.0	332	Died

Obstruction at the same point was produced in second group of six dogs. After the toxemia was well established, as evidenced by the clinical appearance and blood chemistry, a lateral anastomosis was performed between the obstructed loop and the collapsed bowel below it (chart 2, table 2). Five of the six animals so treated died as a result of the toxemia and operation. The sixth animal was not really toxic when the obstruction was released. The toxicity developed so rapidly in some of the animals that anastomosis could not offer much chance of survival (dogs 9 and 11). Dogs 10, 12 and 13, however, had a good chance of recovery. In general, it seems fair to conclude that when the toxemia has become well established, surgical procedure alone will not effect a cure. The chances can be much

before operation, obstructions were produced by dividing the jejunum and inverting the ends at a measured distance (10 inches) below Treitz's ligament.<sup>5</sup> Ether anesthesia was employed. Water was allowed when desired following operation, but nothing else was given by mouth. The nonprotein nitrogen and blood chlorides were determined before and every day after the operation, specimens being taken from the jugular vein each morning. The nonprotein nitrogen of the whole blood was determined by the method of Folin and Wu, and the chlorides by a modification of the method of van Slyke. The degree of toxemia was judged from the clinical appearance of the animal and by the increase in the nonprotein nitrogen of the blood. It is not possible to estimate any exact day on which the toxemia will occur, as great variation takes place in this regard. When the dog appeared definitely toxic, and when the nonprotein nitrogen was over 40 mg. per hundred cubic centimeters, the various procedures outlined subsequently

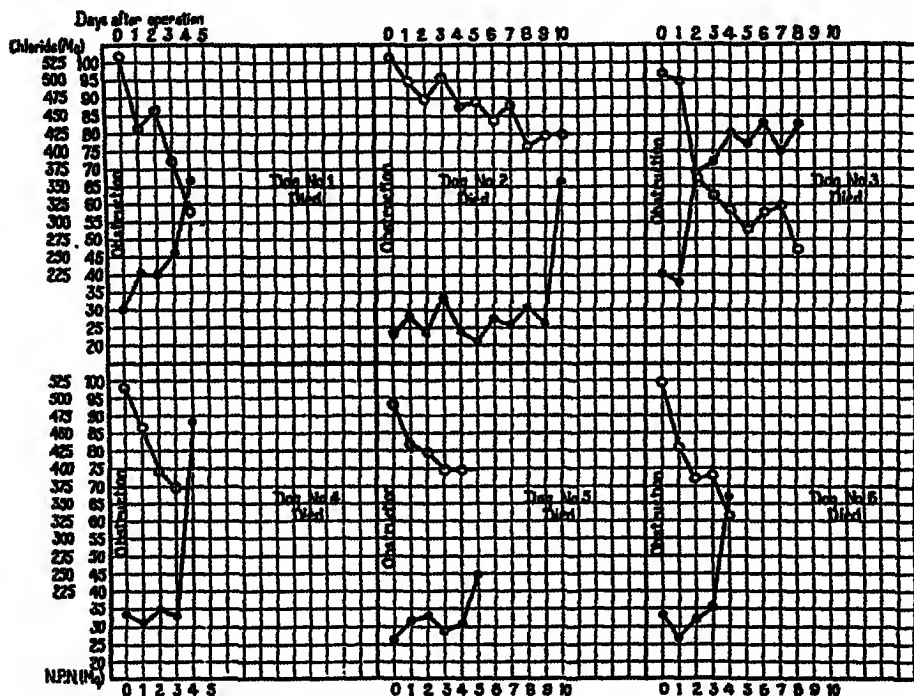


Chart 1.—Results of obstruction of the jejunum in untreated dogs.

were carried out. Operations were invariably performed with the dog under ether anesthesia, and neither fluid nor salt solution was given to the animals, special care being taken to avoid saline on account of the beneficial effects shown by Haden and Orr.<sup>6</sup> The test was made difficult purposely, and it is realized that possibly better results could have been obtained by using local anesthesia, forcing fluids and bringing the salt balance back to normal. In all cases milk was allowed after the release of an obstruction by lateral anastomosis between the loops.

Obstructions were produced by dividing the jejunum and turning in the ends 10 inches below Treitz's ligament. Death occurred in from four to ten days with a rise in the nonprotein nitrogen and a fall in the blood chlorides. This served as the control series (chart 1, table 1). This group does not differ in any

5. The suspensory ligament which marks the transition between the duodenum and the jejunum is referred to as Treitz's ligament throughout this communication.

6. Haden, R. L., and Orr, T. G.: Obstruction of the Jejunum, *Arch. Surg.* 11:859 (Dec.) 1925.



improved by local anesthesia, hypodermoclysis, increase in the sodium chloride and possibly by emptying the obstructed loop of its contents or removing the distention (enterostomy).

Two dogs were given *B. welchii* antitoxin intravenously, the amount being based on 1.5 cc. serum per kilogram of body weight. After this, the bowel was obstructed (chart 3, table 3). Both dogs were slow in developing toxemia and died only after eleven and fourteen days, respectively. The antitoxin seemed to delay the toxic symptoms. Additional experiments of this kind must be carried out.

Eleven dogs were given *B. welchii* antitoxin intravenously and obstructions produced as previously described. After a toxemia was well established, a lateral

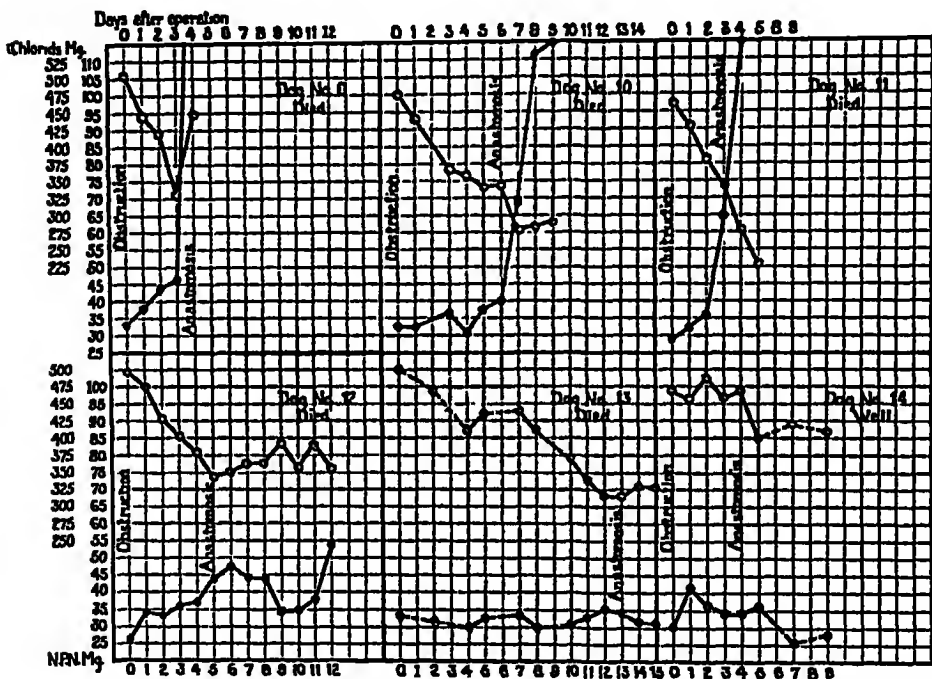


Chart 2.—Results of obstruction of the jejunum with lateral anastomosis after toxemia had been established.

anastomosis was performed to relieve the obstruction, and more *B. welchii* antitoxin was administered (chart 4, table 4). Eight of the eleven animals survived the toxemia and operation and recovered; three animals died. Animals 15, 16, 17 and 18 were treated with a dilute antitoxin, and the results were uniformly successful. After this, the manufacturing company stopped making the dilute antitoxin and supplied only a "concentrated" form. This was the antitoxin used on animals 19, 20, 21 and 22, only one recovering. Whether the concentration of the antitoxin produced this change in the results is not known. Animals 29, 30 and 31 were given the unconcentrated form of the original successful serum, but the unit value was double that of the former. It is the impression that the dogs treated with *B. welchii* antitoxin develop toxemia more slowly after the obstructions are established and that the same animals withstand operation better than normal dogs with obstructions. Haden and Orr<sup>6</sup> showed that when toxemia had been



The results of the operation were as follows: 1. In 10 cases of prostatic hypertrophy, 7 were cured and 3 were not. 2. In 10 cases of prostatic carcinoma, 7 were cured and 3 were not. 3. In 10 cases of radical prostatectomy, 7 were cured and 3 were not. 4. In 10 cases of radical cystectomy, 7 were cured and 3 were not. 5. In 10 cases of radical urethrectomy, 7 were cured and 3 were not. 6. In 10 cases of radical perineal prostatectomy, 7 were cured and 3 were not. 7. In 10 cases of radical perineal cystectomy, 7 were cured and 3 were not. 8. In 10 cases of radical perineal urethrectomy, 7 were cured and 3 were not. 9. In 10 cases of radical perineal prostatectomy and cystectomy, 7 were cured and 3 were not. 10. In 10 cases of radical perineal prostatectomy and urethrectomy, 7 were cured and 3 were not.

The results of the operation were as follows: 1. In 10 cases of prostatic hypertrophy, 7 were cured and 3 were not. 2. In 10 cases of prostatic carcinoma, 7 were cured and 3 were not. 3. In 10 cases of radical prostatectomy, 7 were cured and 3 were not. 4. In 10 cases of radical cystectomy, 7 were cured and 3 were not. 5. In 10 cases of radical urethrectomy, 7 were cured and 3 were not. 6. In 10 cases of radical perineal prostatectomy, 7 were cured and 3 were not. 7. In 10 cases of radical perineal cystectomy, 7 were cured and 3 were not. 8. In 10 cases of radical perineal urethrectomy, 7 were cured and 3 were not. 9. In 10 cases of radical perineal prostatectomy and cystectomy, 7 were cured and 3 were not. 10. In 10 cases of radical perineal prostatectomy and urethrectomy, 7 were cured and 3 were not.

General anesthesia was induced in all cases by a single injection of 10 cc. of a 3 per cent solution of procaine hydrochloride into the sacral space of the sacral canal. Paravertebral injections for blocking the nerves at the sacral foramina on either side, or transsacral

1. Miyata, T., and Kujikawa, H.: Roentgenology of the Male Urethra Especially Prostatic Urethra, J. Oriental Med. 6:31, 1927.  
 2. Herry, G. P.: Caudal Epidural Anesthesia in Perineal Surgery of the Female Genital Tract, J. A. M. A. 90:1018 (March 31) 1928.

TABLE 4.—Obstruction of Jejunum with Lateral Anastomosis After Toxemia Was Established Plus *B. Welchii* (Perfringens) Antitoxin

Dog No.	Day after Operation	Blood, Amount per 100 Cc.		Comment
		Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	
15	0	32.2	408	Antitoxin, 20 cc.; obstruction
	1	29.5	475	
	2	33.4	350	
	3	36.8	307	
	4	37.0	322	
	5	45.4	290	Antitoxin, 20 cc.; lateral anastomosis
	6	51.8	283	
	7	49.2	213	
	8	44.8	269	
	9	....	...	
	10	31.7	286	Well
	11	40.5	283	
	12	30.1	333	
	13	32.4	397	
	14	....	...	
	15	30.0	445	
16	0	31.5	460	Antitoxin, 18 cc.; obstruction
	1	28.6	435	
	2	28.6	460	
	3	27.9	420	
	4	27.5	450	
	5	28.6	415	
	6	34.3	391	
	7	34.3	373	
	8	33.3	320	
	9	33.0	320	
	10	31.1	338	Antitoxin, 15 cc.; lateral anastomosis
	11	42.8	278	
	11½	40.0	310	
	12	66.0	230	
	13	40.3	304	
	14	30.0	...	Well
	15	25.0	402	
17	0	29.2	515	Antitoxin, 18 cc.; obstruction
	1	30.7	445	
	2	29.7	422	
	3	32.4	480	
	4	42.0	400	
	5	55.0	376	Lateral anastomosis Antitoxin, 15 cc.
	6	48.7	421	
	7	47.2	421	
	8	31.6	433	
	9	32.8	453	
	10	29.5	421	Well
	21	31.7	520	
18	0	30.8	400	Antitoxin, 20 cc.; obstruction
	1	28.0	440	
	2	30.0	445	
	3	31.6	445	
	4	....	...	
	5	33.7	445	
	6	33.3	415	
	7	37.5	390	
	8	43.2	375	
	8½	44.0	379	
	9	50.0	393	Antitoxin, 12 cc.; lateral anastomosis
	10	40.0	357	
	11	42.8	420	
	12	40.0	395	
	13	26.0	475	
19	0	30.4	468	Antitoxin, 12 cc.; obstruction
	1	30.0	405	
	2	33.4	405	
	3	35.3	398	
	4	35.4	353	
	5	36.7	317	
	6	33.7	312	
	7	36.8	312	
	8	37.5	300	
	9	40.0	241	
	10	....	...	Antitoxin, 15 cc.; lateral anastomosis Died

# A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

E. STARR JUDD, M.D.

ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.

ROANOKE, VA.

GORDON S. FOULDS, M.D.

TORONTO

JEAN VERBRUGGE, M.D.

ANTWERP, BELGIUM

AND

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

## URETHRA

*Urethrography.*—Miyata and Kajikawa<sup>1</sup> have made forty-four urethrograms in thirty-two cases of normal and pathologic urethras. In some cases material was injected into the bladder and a urethrogram obtained during micturition, and in the others the urethrogram was made during injection of the urethra. They used 40 per cent iodized oil, from 5 to 15 per cent sodium bromide, from 5 to 15 per cent sodium iodide, from 5 to 10 per cent calcium bromide and from 5 to 10 per cent calcium iodide. The 40 per cent iodized oil was found to be satisfactory. The complications in certain cases were intense pain and hematuria, sometimes for two days following injection. The oil, however, did not cause symptoms. Twenty urethrograms are shown and compared to normal cases.

## ANESTHESIA

Berry<sup>2</sup> reported 165 consecutive cases of epidural (caudal) anesthesia in perineal operations on the prostate and seminal tract. The series included 140 cases of perineal prostatectomy and 3 of punch operation for benign prostatic hypertrophy, 16 cases of conservative and 3 of radical perineal prostatectomy for carcinoma of the prostate, and 3 cases of radical excision of the entire seminal tract for tuberculosis.

General anesthesia was induced in all cases by a single injection of 20 cc. of a 3 per cent solution of procaine hydrochloride into the extradural space of the sacral canal. Paravertebral injections for blocking the nerves at the sacral foramina on either side, or transsacral

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1. Miyata, T., and Kajikawa, H.: Roentgenology of the Male Urethra Especially Posterior Urethra, *J. Oriental Med.* 6:31, 1927.

2. Berry, G. P.: Caudal Epidural Anesthesia in Perineal Surgery of the Genito-Urinary Tract, *J. A. M. A.* 90:1018 (March 31) 1928.

obstruction in bringing about the recovery of dogs with obstructions. Control dogs do not recover under similar circumstances.

The antitoxin seems to be specific in its action, as other forms of antitoxin and serum are not effective.

These experiments give only indirect evidence that the toxin of *Bacillus welchii* is concerned. Additional experiments on the direct effect of the toxin are being conducted.

operative work, recommended from 20 to 25 cc. of 2 per cent solution of procaine with the addition of sodium chloride and sodium bicarbonate. Other formulas have been proposed. It has been maintained that the efficiency of the solution is increased by the addition of calcium chloride, and potassium sulphate has been employed for the same purpose. Meeker and Scholl,<sup>5</sup> in a series of 500 cases, added bicarbonate of soda, sulphate, calcium chloride and a number of other drugs to procaine in an endeavor to increase the efficiency of the anesthesia. Their experience has not indicated that the combination of other solutions with procaine results in more satisfactory anesthesia. In their series of more than 1,800 cases of sacral anesthesia including caudal (sometimes called epidural) and complete intrasacral anesthesia, it was found that 1 per cent solution gave a minimal reaction and the most satisfactory and lasting anesthesia. In a series of 585 cases of simple caudal injections reported by Scholl, the most satisfactory results were obtained with a 2 per cent solution in which approximately 0.6 Gm. of procaine was injected. The percentage of failure following simple caudal injection is greatly reduced by injecting the first and second lateral foramina. This also markedly diminishes the time in which the anesthesia appears.

Caudal anesthesia is not new, but its efficiency is particularly marked in such cases as Young described in which operative approach through the perineum is used. It is also a satisfactory anesthesia for rectal work and for perineorrhaphy. The maximal anesthesia, after caudal anesthesia, is obtained in the space between the rectum and the scrotum and between the rectum and the urethra in the female.]

#### CYSTOSCOPIC REACTION

Wehrbein<sup>6</sup> reported a series of 328 cystoscopic examinations by three operators with 63 (19.2 per cent) reactions. The operator having the fewest reactions was the one who possessed unusual skill and gentleness in manipulation and exercised good judgment concerning the length of the procedures. On the other hand, reactions occurred more commonly when the operator insisted on complete investigation, although prolonged and difficult, and considered the patient's discomfort less than did the other operators.

Apparently lesions of the urinary tract have nothing to do with cystoscopic reactions. In 279 such cases reactions occurred in 55 (19.7 per cent). In forty-nine cases without lesions of the urinary tract, reactions occurred in eight (16.3 per cent).

The difference between the percentage of reactions due to pyelographic procedures and to mere ureteral manipulations is not great. There were 20.7 per cent reactions with pyelography and 14.3 per cent

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5. Meeker, W. R., and Scholl, A. J.: Sacral Nerve Block Anesthesia: the Anatomy Involved. Technic and Clinical Application, *Ann. Surg.* 80:739, 1924.

6. Wehrbein, H. L.: Cystoscopy Reactions, *Ann. Surg.* 87:435, 1928.

intradural injections to augment caudal anesthesia, were not used, nor was the extradural injection repeated in case of failure.

Complete abolition of pain following the single injection was secured in 84 per cent of the cases, while in the remaining 16 per cent general anesthesia was required. Serious reactions did not occur, and in 52 per cent of the cases there were no reactions.

Symptoms characteristic of general intoxication from procaine occurred in 10 per cent. The remaining cases showed symptoms secondary to visceral vascular dilatation from paralysis of the sympathetic nerve.

Berry used 20 cc. of 3 per cent solution of procaine and considered that this amount and strength are the most desirable because of absence of any serious reactions.

Young<sup>3</sup> stated that there are several factors to be considered in the choice of anesthetic in prostatic cases. The first of these is the function of the kidneys, as in a large proportion of cases of prostatic hypertrophy there is so much back pressure as to impair renal function. Cardiovascular disorders are also common. In about 3 per cent of the cases the systolic blood pressure was 150 or more. Some form of heart disease was present in almost half of the 198 cases; in many of these, nitrous oxide was distinctly contraindicated.

Young used spinal anesthesia extensively, but has abandoned it because he believed that it is fraught with a certain amount of danger. The region anesthetized is much more extensive than is necessary, and the reactions are dangerous and difficult to counteract. He has used caudal anesthesia since 1924. At first he used a 1 per cent solution, but after a long series of experiments he found that better results and less reaction were obtained by the use of 20 cc. of 3 per cent solution. In a number of cases he was able to carry out his radical operation for carcinoma of the prostate, in which he removed the prostate with the vesical neck, seminal vesicles and ampulla of the vas deferens. The only pain experienced occurred when the vas deferens was reached. To overcome this pain, he now makes a local injection of procaine. There were no operative or anesthetic deaths in 265 cases.

In view of the fact that most of his patients were advanced in years and also that the work of several other men was included, this is an unusual report.

[ED. NOTE.—Both Young and Berry stated that they secured the best results when using 20 cc. of 3 per cent solution. The quantity and percentage strength of the solution varies in the hands of different operators. Lāwen,<sup>4</sup> who first demonstrated its practicability for

3. Young, H. H.: Epidural Caudal Anesthesia in Prostatic Surgery, *J. A. M. A.* 90:1021 (March 31) 1928.

4. Lāwen, A.: Die Extraduralanästhesie, *Ergebn. d. Chir. u. Orth.* 5:39, 1913.

## PAIN IN THE BACK

Kutzmann<sup>8</sup> stated that a significant relationship exists between urologic conditions and pain in the back. He discussed the causes of urologic disorders and described the character and nature of the pains involved. In summarizing, he concluded that the genito-urinary tract plays the chief part in the etiology of pain in the back and that the causes of urologic disorders may be divided into four groups: (1) localized or visceral pain, (2) radiating colic-like pain, (3) referred pain and (4) metastatic pain. He expressed the opinion that the physician should acquire certain preliminary or presumptive evidence before resorting to further urologic procedures.

Hinman, in discussing the paper, noted that the stated conditions may be present often without pain, and that pathognomonic pain of intra-abdominal disease is not present. Certain cases are more characteristic, but the typical pain of appendicitis can be simulated by ureteral stone and vice versa; pain in the gallbladder may be reproduced by renal stone. Hinman also stated, in regard to ureteral pain, that when the pain is referred to the testicles from a lesion in the upper part of the ureter, the tunics of the testicle alone are sensitive, whereas in referred pain in the testicle from lesions lower in the ureter, the skin of the scrotum may also be sensitive. Also the spinal segments supplying the bladder, penis and scrotum are often implicated in referred pain.

## KIDNEY

*Surgical Nephritis.*—Tietze<sup>9</sup> stated that renal decapsulation, until recently, was considered an operation for anuria, threatened oliguria or renal hemorrhage; its use in nephritis was thought problematic. Volhard concluded that the fate of the tubules depended on the circulation of the glomeruli; and gave the following classification:

First Chief Group: Primary parenchymal degeneration (not brought about by a disturbance in glomerular circulation): nephrosis and necrosis.

Infectious nephritides: (1) hemorrhagic nephritis, (2) nephritis dolorosa, (3) embolic nephritis in endocarditis, (4) septic interstitial nephritis (accompanying general sepsis) and (5) hematogenous pus in the kidneys.

Second Chief Group: The disturbance of the glomerular circulation functionally, that is, angiospastic, depends on: (1) acute diffuse glomerulonephritis; (2) the kidney in eclampsia and during pregnancy, and (3) incipient lead poisoning of the kidney.

The disturbance of the glomerular circulation organically depends on: (1) the chronic, that is, unhealed glomerulonephritis in its various

8. Kutzmann, A. A.: Back Pain of Urologic Origin, *California & West. Med.* 27:208, 1927.

9. Tietze, Alexander: Erfahrungen mit der Nierendekapsulation, *Beitr. z. klin. Chir.* 139:88, 1927.

with ureteral manipulations. Five of twelve double pyelograms (41.7 per cent) were followed by reactions. This not only points to the inadvisability of making double pyelograms, but accentuates the fact, previously mentioned, that the pyelogram per se represents an additional injury.

Wehrbein concluded that the presence of infectious organisms and trauma are the most significant factors in the causation of reactions following cystoscopy. Elevation of the temperature and injection of the urinary tract, with the exception of acute prostatitis, are not absolute or even common contraindications to cystoscopy.

#### CHEMISTRY OF THE BLOOD

Bandler and Killian<sup>7</sup> reviewed extensively the value of chemical analysis of the blood in urologic cases. Various methods were discussed and the results of chemical analyses were reported in eleven cases which represent various degrees of renal impairment due to lesions in the urinary tract. The practical value of chemical analysis of the blood was discussed in relation to a determination of the therapeutic measures to be employed. Cases 1 and 2 illustrate the improvement of renal function that follows relief of urinary obstruction and the increase in the volume output of urine caused by forcing fluids. In the second case, failure to relieve the obstruction by catheterization signified the necessity of immediate surgical intervention despite the elevation of the blood urea nitrogen. The preoperative improvement in renal function diminished the surgical risk, and failure to utilize the data obtained in chemical analyses as an index to treatment increased the surgical risk. Increasing the fluid intake did not appreciably influence the retention of nitrogen in the blood unless the urinary obstruction was removed.

In cases showing nitrogen retention, the prognosis, whether from a surgical or medical standpoint, should be based not on the concentration of any one nitrogenous waste product in the blood, but rather on the relative concentration of urea nitrogen and of the creatinine. When the retention of nitrogen in the blood is due to mechanical obstruction, a rise in urea nitrogen and creatinine to the same extent is observed. In chronic renal impairment, however, a relatively greater concentration of creatinine than of the urea nitrogen is noted. Analogous changes in the chemical composition of the blood are observed in cases of mechanical obstruction in the urinary tract, whether this obstruction occurs in the urethra, in the bladder, in the ureters or in the kidneys. The retention of nitrogen observed after obstruction of one ureter is as great as in bilateral ureteral obstruction. This observation has been corroborated by animal experiments.

7. Bandler, C. G., and Killian, J. A.: *The Practical Value of Chemical Analysis of the Blood in Urological Conditions*, J. Urol. 19:1, 1928.



## PAIN IN THE BACK

Kutzmann<sup>8</sup> stated that a significant relationship exists between urologic conditions and pain in the back. He discussed the causes of urologic disorders and described the character and nature of the pains involved. In summarizing, he concluded that the genito-urinary tract plays the chief part in the etiology of pain in the back and that the causes of urologic disorders may be divided into four groups: (1) localized or visceral pain, (2) radiating colic-like pain, (3) referred pain and (4) metastatic pain. He expressed the opinion that the physician should acquire certain preliminary or presumptive evidence before resorting to further urologic procedures.

Hinman, in discussing the paper, noted that the stated conditions may be present often without pain, and that pathognomonic pain of intra-abdominal disease is not present. Certain cases are more characteristic, but the typical pain of appendicitis can be simulated by ureteral stone and vice versa; pain in the gallbladder may be reproduced by renal stone. Hinman also stated, in regard to ureteral pain, that when the pain is referred to the testicles from a lesion in the upper part of the ureter, the tunics of the testicle alone are sensitive, whereas in referred pain in the testicle from lesions lower in the ureter, the skin of the scrotum may also be sensitive. Also the spinal segments supplying the bladder, penis and scrotum are often implicated in referred pain.

## KIDNEY

*Surgical Nephritis.*—Tietze<sup>9</sup> stated that renal decapsulation, until recently, was considered an operation for anuria, threatened oliguria or renal hemorrhage; its use in nephritis was thought problematic. Volhard concluded that the fate of the tubules depended on the circulation of the glomeruli, and gave the following classification:

First Chief Group: Primary parenchymal degeneration (not brought about by a disturbance in glomerular circulation): nephrosis and necrosis.

Infectious nephritides: (1) hemorrhagic nephritis, (2) nephritis dolorosa, (3) embolic nephritis in endocarditis, (4) septic interstitial nephritis (accompanying general sepsis) and (5) hematogenous pus in the kidneys.

Second Chief Group: The disturbance of the glomerular circulation functionally, that is, angiospastic, depends on: (1) acute diffuse glomerulonephritis; (2) the kidney in eclampsia and during pregnancy, and (3) incipient lead poisoning of the kidney.

The disturbance of the glomerular circulation organically depends on: (1) the chronic, that is, unhealed glomerulonephritis in its various

8. Kutzmann, A. A.: Back Pain of Urologic Origin, California & West. Med. 27:208, 1927.

9. Tietze, Alexander: Erfahrungen mit der Nierendekapsulation, Beitr. z. klin. Chir. 139:88, 1927.

stages of glomerular circulation disturbance, leading to early renal insufficiency (subacute course of extracapillary nephritis); the sub-chronic course of intracapillary nephritis disguised by the picture of earlier chronic parenchymal nephritis; a third chronic course simulating the picture of chronic interstitial nephritis; (2) renal sclerosis and true contracted kidney, and (3) amyloid kidney.

The success of decapsulation, according to this classification and as performed by Kümmel, was not noted in nephrosis except in unusual cases, and in necrosis the operation was carried out in cases of anuria with poor results.

The more remarkable results were with the infectious nephritides; bleeding ceased, pains disappeared and the infected kidneys recovered.

In the second chief group, the results in cases of anuria, acute nephritis and eclampsia, such as resumption of urinary flow and rapid recovery from renal disease, were phenomenal. There were, however, some failures.

In the really chronic nephritides or organic disturbances of the renal circulation, Volhard did not note a successful result.

Tietze next mentioned the work of Edebohls and Rovsing, both of whom advocated decapsulation on the theory of renewed circulation from the adjacent tissues.

In conclusion, Tietze stated that the operation of decapsulation is still worthy of consideration even though its indications in the foregoing conditions may be limited.

[ED. NOTE.—A number of reports of operation in cases of nephritis have been published recently. Rovsing<sup>10</sup> reported a series of 157 cases, of which 77 were his own. Thus, fifty-three of sixty-two patients with interstitial nephritis were cured following decapsulation; eight were improved and one died. Of fifty-six patients with granular nephritis, twenty-four were cured, twenty-one were improved, two remained the same and nine died. Eight of twenty-four patients with nephrosis were cured, nine were improved, four remained the same and three died. Of nine patients with glomerulonephritis, four were cured, four were improved, and one remained the same. These patients of Rovsing were operated on during a period of thirteen years. The operative procedure carried out in most of his cases was nephrolysis, that is, shelling the kidney out from its capsule of fat and connective tissue. This operation is carried out through a lumbar incision; the kidney is stripped from its fatty capsule; the *membrana propria* is lifted and incised near the convexity of the kidney and stripped off by means of blunt dissection to the renal hilum.

10. Rovsing, T.: *Chirurgische Behandlung der Nephritiden*, Verhandl. d. Dän. Med. Ges. 10:23, 1922-1923.

Kümmell<sup>11</sup> stated that the good effect of decapsulation is probably due to the removal of the fibers of the sympathetic nerve which are severed from the kidney by the removal of the capsule. The establishment of collateral circulation and the formation of a new capsule, which takes place rather readily, can account only in part for the favorable results. Kümmell reviewed the clinical results of his cases of nephritis in which either nephrotomy or decapsulation was carried out. Nine of forty-two cases in which operation was performed were associated with nephritis dolorosa. Nephrotomy was performed in fifteen, nephrectomy in three, and decapsulation in twenty-four cases. Fifteen of the twenty-four patients were dismissed as almost cured, eight as improved, and one died fourteen days after operation from pneumonia.

Quinby<sup>12</sup> reported three cases of decapsulation for various forms of nephritis treated at the Peter Bent Brigham Hospital; one was a case of hemorrhagic nephritis, one of acute tubular nephritis, and one of chronic glomerulonephritis with edema. After bilateral decapsulation the patients were observed carefully with respect to chemical changes in the blood as well as other more general observations; none of them derived any benefit.

Few reports on nephritis have been published in this country, and these, like Quinby's, do not reflect the general optimism of the reports of Rovsing, Kümmell and Damski from European clinics. Apparently this operation is performed frequently in urologic centers in Europe. It offers enough possibilities to be considered at least in certain types of cases in our urologic clinics.]

*Renal Stones.*—Beer<sup>13</sup> stated that, before considering operative intervention in the treatment of renal stones, it is necessary to know whether or not the patient's kidney is infected, whether it is sufficiently preserved to be of future service, whether the other kidney is able to support life should nephrectomy be necessary, and whether the involved kidney is the only one the patient possesses. In regard to infection, if a renal stone is removed by nephrotomy, sutures passing through such a kidney may lead to secondary widespread infection, so that nephrectomy is necessary later. If the stone is in a solitary kidney, the kidney should be handled carefully and not removed from its normal position, the operation being performed in situ. On the other hand, if functional tests show that the organ is markedly destroyed and full of pus, unless adequate parenchyma is found, nephrectomy may be advisable.

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11. Kümmell, H.: Die chirurgische Behandlung der Nephritis, *Ztschr. f. urol. Chir.* 17:27, 1925.

12. Quinby, W. C.: A Note on the Results of Decapsulation of the Kidney for Various Forms of Nephritis, *J. Urol.* 13:321, 1925.

13. Beer, Edwin: Points in the Technic of Operative Removal of Kidney Stones, *Ann. Surg.* 87:428, 1928.

stages of glomerular circulation disturbance, leading to early renal insufficiency (subacute course of extracapillary nephritis); the sub-chronic course of intracapillary nephritis disguised by the picture of earlier chronic parenchymal nephritis; a third chronic course simulating the picture of chronic interstitial nephritis; (2) renal sclerosis and true contracted kidney, and (3) amyloid kidney.

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10. Rovsing, T.: *Chirurgische Behandlung der Nephritiden*, Verhandl. d. Dän. Med. Ges. 10:23, 1922-1923.

bleeding from the renal parenchyma. This is done by putting a soft rubber tube about the renal pedicle, crossing the two loops of rubber tube on the anterior surface of the pedicle, and at the crossing placing an artery forceps.

In cases in which the capsule is stripped from the parenchyma in delivering the organ, it is necessary to remember that in performing pyelotomy the reflected capsule, the adherent perinephric fat, the fat surrounding the kidney, and finally the pelvis itself must be cut through before the stone is reached.

After performing pyelolithotomy, it is immaterial whether or not the pelvis is carefully closed by sutures. In some cases the pelvic incision will not leak even though closure is not made; on the other hand, some pelves which have been carefully sutured leak freely.

*Hydronephrosis.*—The infrequency of dystocia because of a misplaced kidney prompted Idel<sup>14</sup> to report the case of a woman, aged 34, who had had six spontaneous deliveries, the last four years previously. Examination revealed dystocia due to a pelvic tumor which was thought to be an ovarian cyst. Cesarean section was performed. Following delivery, the uterus was repaired and pushed anteriorly. A large cystic tumor was found retroperitoneally occupying the pouch of Douglas. It was the size of a child's head, with a capacity of 2 liters. It was ruptured during removal, with loss of a great deal of blood. The patient died, and necropsy revealed hydronephrosis in a left unilateral fused kidney at the level of the sacrum.

Maximovitch<sup>15</sup> discussed the question of plastic operations for hydronephrosis and reported 112 cases. Fifty-two of the patients were men and sixty were women. Hydronephrosis was complete in 104 cases and partial in 8 cases. Infection was present in fifty-six cases and was not present in fifty-six.

The cause was stricture, kink, anomaly, tumor, atony, etc., in fifty cases, stones in forty-seven, tuberculosis in five and not determined in ten.

Nephrectomy was performed in sixty-seven cases, nephrostomy in twenty and plastic operations in twenty-four (neostomy in five, plastic operation and straightening of the ureter in ten, and pelvic resection, with plication in nine).

One hundred and three patients recovered, and nine (8.7 per cent) died. The treatment of hydronephrosis may be either conservative or operative. The former consists of pelvic lavage, which may control an inflammatory process and cause some contraction of a dilated pelvis.

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14. Idel, August: Hydronephrose einer dystopen Verschmelzungsniere als Geburtshindernis, Zentralbl. f. Gynäk. 51:2913, 1927.

15. Maximovitch, A. S.: Ueber plastische Operationen bei der Hydronephrosis, Ztschr. f. urol. Chir. 23:383, 1927.

In Beer's series of 271 cases of renal stone, he found that in 18 per cent the kidneys were so badly destroyed that it was inadvisable to save the organ. In 5 per cent of the cases, either the other kidney was diseased or the stone was in a solitary kidney, so that it was necessary to remove the stone without dislocating the organ. In the remainder of the cases, Beer's choice of operation was pyelotomy or nephrotomy, or a combination of the two. In recent years, pyelotomy has become the more popular type of operation. In Beer's last series of thirty-eight cases, nephrolithotomy was performed in one, nephrectomy in eight, and pyelolithotomy or combined pyelonephrolithotomy in the remainder. Incision into the pelvis spares the parenchyma of the kidney.

Beer exposes the kidney adequately by means of an inverted "S" incision in the lumbar region which begins close to the eleventh rib at the margin of the erector muscle; it then passes obliquely down through the lumbar space between the crest of the ilium and the last rib. Paralleling the last rib, it should extend forward and downward in front of the anterior spine as far as is necessary to get an adequate approach. The kidney being exposed through this incision is gradually liberated from its perinephric fat; adhesions to the upper pole should be carefully ligated before being cut, and then the kidney can usually be completely liberated and dislocated unless there are contraindications to this procedure. This usually permits the operator to raise the organ well up to the muscular or skin plane. After the kidney is exposed in this way, the ureter should be exposed as a routine and a double loop of heavy catgut should be thrown around the ureter to constrict its lumen, which prevents fragments which may break off from the stone or stones slipping into the ureter, and subsequently causing obstruction or symptoms due to the existence of fragments in either the lumbar or the pelvic ureter.

When the kidney is well exposed, most stones can readily be removed by a posterior pyelotomy incision. Abnormal vessels can usually be pushed aside. At times very large and distorted stones can be readily removed through an incision in the renal pelvis.

After a renal stone is removed, Beer washes out the organ with a strong stream of water introduced through a large catheter, so as to clean out any sand or fragments. Beer has not found fluoroscopy of the kidney at the operating table entirely satisfactory. At times small stones have been removed from the kidney directly after the fluoroscopic examination had shown that the kidney did not harbor more calculi. He carries out Quinby's system of taking pictures of the kidney for immediate development. This procedure is carried out in all his cases, except in those with single small stones.

If the pyelotomy approach is impossible, nephrolithotomy may be necessary. If wide nephrotomy is performed, it is well to control the

Hydronephrosis secondary to aberrant vessels is characterized by intermittent, regular attacks of renal pain occurring over a period of months or years, usually in the young adult.

It occurs most frequently in patients predisposed to movable kidney who present a peculiar form of the body consisting of an elongated thorax, with a small abdominal circumference in which the paravertebral fossa is shallow, cylindrical or funnel-shaped. Because of the rôle played by renal mobility, it is more common in women, on the right side.

The kink in the ureter can be demonstrated by a proper ureteropyelogram in the vertical position. The dilatation of the ureter and pelvis always commences just above the point of obstruction by the vessel. The enlarged kidney can be palpated in about 40 per cent of the cases.

When conservative measures fail to relieve symptoms, surgical intervention should be resorted to. In early cases division of the vessel and suspension of the kidney will suffice. In the more advanced type presenting the narrowing of the ureteropelvic juncture, it is necessary to widen by plastic operation. In badly infected hydronephrotic kidneys and in those presenting advanced destruction, nephrectomy is the treatment of choice.

Good results were obtained from surgical intervention. In a group of eleven patients who received surgical treatment, there was complete relief of symptoms.

It behooves the urologist, internist and general surgeon to recognize the clinical entity of the particular type of movable kidney which, when it descends over an aberrant vessel, causes marked disturbances and symptoms.

Fabian<sup>17</sup> reported a case of carcinoma of the bladder which did not produce any local symptoms except a hemorrhage. The growth occluded the outlet of the right ureter and led to hydronephrosis with pyelitis, which in turn caused ileus. The outlet of the bladder was so narrowed that cystoscopy was impossible. Tumor was felt on rectal examination and was mistaken for prostatitis. On admission to the hospital, symptoms of ileus dominated the picture, but obstruction in the intestine was not found at operation. The true nature of the condition was made clear by the sudden rapid growth of the tumor. The patient, a man, aged 36, died two months after the first appearance of symptoms in the abdomen and the region of the kidney.

*Renal Anomalies.*—MacKenzie and Hawthorne<sup>18</sup> reported a series of six cases of unilateral renal aplasia. Five of the patients are living.

17. Fabian, K.: Blasenerkrankung mit ileusartigen Erscheinungen, Zentralbl. f. Chir. 54:983, 1927.

18. MacKenzie, D. W., and Hawthorne, A. B.: Unilateral Renal Aplasia. Surg. Gynec. Obst. 46:42, 1928.

The presence of ureteral stricture should indicate dilatation with bougies. In certain cases operation should not be performed, such as cases of a large, enclosed aseptic hydronephrotic sac of long duration, especially if the removal by changing the intrathoracic pressure would increase the danger of the anesthetic. In the removal of large kidneys, the size of the operative wound and the trauma may cause emboli.

The operative treatment of hydronephrosis may constitute: (1) a procedure which removes the cause of the hydronephrosis and restores renal function, (2) palliative openings into the hydronephrotic sac and (3) nephrectomy.

Plastic operations are employed to eliminate etiologic factors such as strictures, kinks and growths. The methods are various and manifold. Plastic operations on the renal pelvis and ureter are at times satisfactory. Plastic operations necessitate an efficient and careful technic and must be carried out with meticulous care. Sutures and edges of wounds must be carefully handled if successful healing is to be realized. At best, the results of plastic work are problematic even when complications do not occur and the operation has been technically successful. In the experience of Maximovitsch's clinic, lateral anastomosis has been the least successful, as determined by secondary operation or necropsy.

Maximovitsch believed that sufficient time has not been allowed to determine the results which may occur in this field of surgery. According to him, this type of work has a great future, which has not yet been fully developed.

Mathé<sup>16</sup> has made a plea for early relief by conservative operation for hydronephrosis secondary to aberrant renal vessels with movable kidney or kinking of the ureter.

The renal blood vessels are irregular in distribution and present numerous varieties and anomalies. This is explained by the fact that there may be multiple renal arteries and veins with every conceivable type of branching, depending on the selection of the channels from the embryonic periaortic plexus. Retention of a portion of the normal renal vascular relations of the embryo before the ascent of the mesonephros into the renal fossa may occur.

Most of the anomalous vessels do not cause obstructive symptoms and do not require treatment. In a certain percentage of cases, renal mobility may cause the ureter to sag or hang over a fixed support consisting of an aberrant vessel which leads to mechanical factors and causes obstruction and hydronephrosis.

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16. Mathé, C. P.: The Rôle of Aberrant Vessels in the Production of Hydronephrosis, *J. Urol.* 19:211, 1928.



may cause rupture of the kidney if it is in a state of hydraulic tension; (3) most traumatic ruptures heal without surgical intervention, but the patient should be hospitalized and carefully observed until hematuria subsides; (4) most ruptured kidneys which require operation may be saved by palliative operation; nephrectomy is seldom necessary; (5) the symptoms of ruptured kidney are usually definite but may be mistaken for intraperitoneal lesions; (6) cystoscopy usually is not necessary for diagnosis, but should be done occasionally to determine the condition of the injured kidney; (7) pyelography is an aid to accurate diagnosis in selected cases; (8) moderate leukocytosis (13,000 to 18,000) may not indicate infection, but absorption of the blood clot and secondary anemia; (9) it is safer to investigate doubtful cases under regional anesthesia than to treat them expectantly; (10) operative procedure is indicated to prevent exsanguination, extravasation and infection, and (11) the morbidity incident to a ruptured kidney is more dependent on the state of shock and subsequent infection than on the amount of secondary hemorrhage.

*Paranephritic Abscess.*—Chwalla<sup>21</sup> defined paranephritic abscess as acute suppurative inflammation of the fatty renal capsule or of the renal fascia. Infection takes place either through an embolic metastatic process or by extension from the kidney or adjacent organs. Most authors believe that it originates in a metastatic abscess of the cortex of an otherwise normal kidney. These abscesses can perforate into the loose pararenal tissue, or infection can take place through the lymph channels. Staphylococcus is the organism most frequently found. Trauma plays a part in a number of cases, probably by producing hematoma in the fatty tissue with subsequent infection. It is difficult to determine whether or not the kidney is involved in the paranephritic process. The diagnostic importance of recent staphylococcus infection, such as furuncle, carbuncle, felon or sore throat, is emphasized. In two thirds of the cases, etiologic factors cannot be elicited. Urinalysis does not aid materially in determining concomitant renal involvement. Normal urine suggests primary metastatic paranephritis; urine which is not normal is suggestive of renal abscess. Nevertheless, all urinary conditions, including anuria of the involved side, may be secondarily induced by paranephritic abscess without the participation of the kidney itself.

Chwalla considered exploratory puncture permissible. The most significant disease from a differential diagnostic standpoint is suppurative retrocecal appendicitis. He is opposed to the more radical methods of exposure, and even removal of the kidney itself. Thirty of his thirty-two patients recovered after simple incision and drainage.

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21. Chwalla, Rudolf: Zur Klinik des paranephritischen Abscesses, *Ztschr. f. urol. Chir.* 23:339, 1927.

and the sixth was examined clinically before death. The diseases ranged from complete absence of a kidney in one case to hypoplasia in two others.

Complete absence of the kidney was reported by Anders in about one case in 1,800, and by Motzfeld in one case in 1,000. Many of these patients showed some abnormality in the genital tract. Moore's statistics showed that 75 of 226 patients examined (33 per cent) had congenital defects of the genital organs. The ureter is completely absent in the majority of cases.

The diagnosis of renal aplasia is important to the urologist. The stress of carrying on all the excretory functions is sometimes sufficient to injure the remaining kidney. Nephritis, the formation of calculus or infection is often found. Ballowitz stressed the frequency of calculi in the solitary kidney, while the combined statistics of Ballowitz, Moore and Anders indicate that a greater than the normal percentage of persons with congenital single kidney die from diseases of the kidney. In 42 per cent of Ander's cases, the single kidney showed advanced lesions of chronic nephritis. Apparently the aplastic condition was more common on the left side than on the right. The aplastic kidneys in this series were all functionless.

Caraven<sup>19</sup> cited a case of horseshoe kidney in a Spaniard, aged 37, with acute ileus. For several days he had noticed a painless tumor in the right lower quadrant. An abdominal incision was made and about 1.5 liters of pus were evacuated from immediately underneath the right abdominal wall. Urine was demonstrated in this material, and an ectopic area of hydronephrosis was found and drained. Cystoscopic and roentgen-ray examinations suggested a provisional diagnosis of pelvic horseshoe kidney. The left side was found intact, and the pyonephrotic part of the horseshoe kidney was removed. There was a urinary fistula which closed in twelve days. The patient recovered.

*Ruptured Kidney.*—Delzell and Harrah<sup>20</sup> reported a series of eleven cases of ruptured kidney, and emphasized the importance of pyelography in the diagnosis and treatment. The hemorrhage following either traumatic or spontaneous rupture of the kidney may result in extensive secondary lesion, usually with marked extravasation and infection. The future economic welfare of the patient is jeopardized.

The authors concluded that : (1) spontaneous rupture of the kidney is rare and occurs only in the presence of lesions; (2) light trauma

19. Caraven, M.: Obstruction intestinale par hydro-pyonephrose dans un rein en fer à cheval ectopique; néphrostomie transpéritonéale; guérison de l'obstruction: Heminephrectomie secondaire et guérison définitive, Bull. et mém. de la soc. nat. de chir. 53:905, 1927.

20. Delzell, W. R., and Harrah, F. W.: Eleven Cases of . . . Kidney, J. Urol. 19:131, 1928.

kidney was good, and the patient had just been through a normal pregnancy. The immediate results following operation were satisfactory.

[ED. NOTE.—In this case the kidney was removed because it was thought to contain a tumor. It was found to be polycystic. Almost invariably, in cases of polycystic disease, one kidney is larger than the other. Removal of the larger kidney, while it relieves the pain, discomfort and abdominal distention, is usually followed by an increase in size of the remaining kidney. There is usually such a small amount of combined renal tissue in the two kidneys that it is necessary to be conservative. Rovsing's operation, which consists of puncturing the various cysts, has given the best results of any operation for polycystic kidney. This procedure is conservative and causes only slight trauma to the kidney. It can be repeated on the other kidney if necessary. Rovsing reported excellent results from this operation.]

*Renal Tumors.*—Stoeckel<sup>26</sup> reported a case of a primipara, aged 33, with a large, right, renal tumor. He saw the patient in the ninth month of pregnancy. The abdominal wall was slightly edematous and the urine scanty. Ureteral catheterization revealed the right ureter to be patent. There was no secretion from the right kidney. He concluded that a closed hydronephrotic sac was present. The patient became progressively worse, as pressure against the diaphragm caused orthopnea and pre-uremic symptoms. One week later, bags were inserted, resulting in spontaneous delivery. The puerperium was normal. On the tenth day, the patient had a coughing spell and then complained that the tumor had burst. Examination showed it to be smaller than previously. There was a rise in pulse and temperature with abdominal distention. Exploratory laparotomy revealed an inoperable tumor in the upper pole of the right kidney. Subsequently, Stoeckel performed a radical operation with complete removal of the tumor. The patient recovered readily from the operation and was well four years later.

Stoeckel expressed the belief that the operation should have been performed earlier. He stated that the risk from nephrectomy is small, and in a case such as this should be carried out as soon as the diagnosis is made. The tumor was grossly cystic. Pathologic study showed it to be a malignant osteo-adenopapilloma destruens, presumably of the kidney.

Lower and Belcher<sup>27</sup> reported the case of a lipoma in the left kidney in a woman aged 52. The patient complained of pain in the abdomen, contraction of the rectum, indigestion and nervousness. A

26. Stoeckel, W.: Maligner Nierentumor (Osteo-Adeno-Papilloma destruens) und Schwangerschaft, *Zentralbl. f. Gynäk.* 51:2906, 1927.

27. Lower, W. E., and Belcher, G. W.: Massive Lipoma of the Kidney with Report of a Case. *Surg. Gynec. Obst.* 45:1, 1927.

**Renal Tuberculosis.**—Fédoroff<sup>22</sup> stated that renal tuberculosis usually develops from a blood-borne infection. In most cases the diagnosis is not difficult, as it is based on clinical symptoms and examination of the urine. The treatment consists of nephrectomy. Bilateral infection is the only contraindication to nephrectomy. The immediate operative mortality is about 4 per cent, while the late mortality varies from 13 to 29 per cent. From 60 to 70 per cent of patients should be cured.

Salleras and von der Becke<sup>23</sup> stated that of a series of 1,724 patients with urologic lesions, 278 (16.1 per cent) had renal tuberculosis. The percentage varied from 8.8 to 28 in different hospitals. Cases in which there is hematuria are less common than those in which the chief symptoms are in the bladder. Any spontaneous cystitis must be regarded as due to tuberculosis until proved otherwise. The early cases without any bacilli are the most difficult to diagnose; the others are diagnosed readily. Cystoscopy and catheterization are valuable aids. The prognosis is not unfavorable if surgical treatment is applied promptly. The death rate from operation varied from 0 to 50 per cent, the average being from 5 to 10 per cent. Deaths had not occurred immediately following operation for four years, and only one late death had occurred from pulmonary tuberculosis. Some of their cases date back thirteen years. If the case is advanced, three to four years must elapse before cure can be considered.

Orth<sup>24</sup> stated that in cases of extensive tuberculosis in one kidney and toxic nephritis in the other, removal of the tuberculous kidney permits the other to return to normal. If the second kidney is also infected, it does not return to normal. It is always important to study carefully the remaining kidney and to follow the course of the case. In bilateral tuberculosis, surgery is not indicated.

**Polycystic Kidney.**—Séjournet<sup>25</sup> stated that association of bilateral pyelonephritis with polycystic kidney usually precludes the possibility of operation. He reported one case in which he performed nephrectomy, and at the end of two years the patient is apparently cured. Nephrectomy was performed on account of the increase in size of one kidney. Hemorrhage and infection were not present, but there was increasingly severe pain in this region. The function of the other

22. Fédoroff: *Tuberculose Urinaire*, J. d'urolog. 24:463, 1927.

23. Salleras, J., and von der Becke, A.: *La tuberculosis renal en la República Argentina*, Rev. Asoc. méd. argent. 40:935, 1927.

24. Orth, Oscar: *Klinische Erfahrungen bei Tuberkulose der einen und toxischer Nephritis der anderen Niere*, Ztschr. f. urol. Chir. 23:435, 1927.

25. Séjournet, M. P.: *Reins polykystiques*, Bull. et mém. Soc. de chir. de Par. 19:654, 1927.

Colston<sup>28</sup> reported an unusual case in which a solitary cyst was found coincidentally with a papillary cystadenoma in the same kidney. The case reported is that of a man, aged 58, who had a three months' history of profuse hematuria. The hematuria was not terminal at any time. General examination did not reveal gross abnormality. Cystoscopic examination showed that the blood was coming from the right kidney. A pyelogram of the right kidney showed a characteristic deformity in the upper calix. A diagnosis of a right renal tumor was made.

At operation, nephrectomy was performed. The specimen showed papillary cystadenoma of the upper pole and a large solitary cyst of the lower pole.

Quinby,<sup>29</sup> on reviewing the end-results of cases of renal tumor in which the patients were treated in the urologic service of the Peter Bent Brigham Hospital, found an unexplained difference between the duration of life after operation and the time when metastasis became apparent. Excluding all cases in which the growth was found to be invasive, as well as those in which lymph nodes about the renal pedicle and aorta were found the seat of secondary deposit, there still lacked evidence on which to base an opinion as to the clinical prognosis. In many cases in which roentgenograms of the lungs and bones have been carefully studied for metastasis before operation and in which the localized character of the tumor as seen at operation gave every hope of cure or at least long freedom from metastasis, death has taken place at a relatively short period after operation.

Of a group of forty-three cases on record at the time this investigation was undertaken, there were thirty-five in which intensive pathologic study was possible.

There is no adequate pathologic criterion on which to base a prognosis on the duration of life after nephrectomy for renal neoplasm. The size of a renal tumor is not a reliable indication of the character in respect to the degree of malignancy. Occasionally, an entirely benign adenoma may become large. Primary ligation of the vascular pedicle by transperitoneal approach is the most logical method of treatment.

[ED. NOTE.—From a review of the case reports as recorded by Quinby, it is found that he does not follow closely the accepted classification laid down by Ewing. Types of cells are frequently recorded as mixed in a given tumor, such as granular, clear, and spindle. Clear polyhedral cell tumors are generally much less malignant than either granular or spindle cell growths. If the tumors described in his reports

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28. Colston, J. A. C.: Solitary Cyst and Papillary Cystadenoma Occurring Simultaneously in One Kidney, *J. Urol.* 19:285, 1928.

29. Quinby, W. C.: Renal Tumors: A Clinico-Pathological Study, *J. Urol.* 19:265, 1928.

left pyelogram showed deformity strongly suggestive of a new growth. At operation, the kidney was found to contain a large subcapsular, friable, yellow tumor resembling hypernephroma. Pathologic examination showed that the mass weighed 420 Gm. In the middle on the lateral surface of the kidney was a large subcapsular, globular mass which appeared yellow through the capsule. On section, it was fatty and mottled. In view of the tendency of these growths to local recurrence, roentgen-ray treatments were given. The patient was doing well six months later.

True lipomas of the kidney may be distinguished from lipomatous masses around the pelvis, which occur in atrophic disease of the kidney (Virchow) and from the enormous perirenal tumors first described by Salzer. True lipomas arise in two sites, under the surface of the renal capsule and at the hilum. The pelvic lipoma may be an extension from the cortical growth. Lipomas in the kidney are rare. Before the diagnosis is made it should be ascertained by microscopic examination that the suspected growths are not adenomas or suprarenal rests. As a rule the lipomas are small, but five cases have been reported in which they were of considerable size. Degeneration of lipomas or the replacement of normal tissue by lipomatosis secondary to calculus, tuberculosis, inflammatory atrophy or operative trauma is not rare. These fatty masses arise from fat around the pelvis.

The symptoms, as a rule, are pressure, pain or discomfort in the region affected. Hematuria is seldom encountered. Lipomas occur in middle age. The patients in all of the reported cases were women. The diagnosis of tumor may be made by the pyelogram. The only treatment is the removal of the tumor by nephrectomy, which should be followed by roentgen-ray treatment. The tumors are prone to recur, and at each recurrence are more cellular in type, ultimately assuming sarcomatous characteristics. This is the sixth case of true lipoma to be presented and the fourth to be removed by nephrectomy.

[ED. NOTE.—Lower and Belcher<sup>27</sup> called attention to another type of lipid growth in the region of the kidney. Fatty degeneration, hypernephroma and suprarenal rests are well known, but subcapsular lipoma is indeed a pathologic rarity. The tendency of these fatty tumors to malignant degeneration in the region of the kidney when such masses elsewhere are usually benign is worthy of note. Again, it will be recalled that this is the site of hypernephroma, a much misunderstood tumor of lipid characteristics. One wonders why lipid tumors in general in the region of the kidney are so prone to recur, to become malignant and to spread in a way that causes confusion with regard to their classification as sarcomatous (mesothelial) or carcinomatous (epithelial).]

vary from minute patches in the mucosa to papillomatous proliferations. They may cause hematuria or favor persistent infection; when occurring in portions of the urinary tract inaccessible to inspection, they may be easily confused with neoplasms.

Granulomas occurring in the kidney are rarely of much clinical significance except that they may be the cause of hematuria in hydronephrosis, chronic pyelonephritis and nephrolithiasis. Although there are a number of factors which may cause hematuria in hydronephrosis, granulomatous areas are occasionally observed in the pelvic mucosa when the hydronephrotic sac is opened. These areas are usually dark red, bleed easily with trauma, and appear to have a low papillomatous structure. More rarely they are present as single or multiple large polypoid growths and, while usually situated at the ureteropelvic juncture, they may be scattered over the entire pelvis.

Microscopic examination will reveal inflammatory hyperplasia of the mucosa and submucosa. Hematuria occurring with chronic pyelonephritis may also result from a similar type of granuloma in the pelvis or ureter. With chronic pyelonephritis, the granulomas may be more marked and the mucosal proliferation more predominant, a condition often called pyelitis granulosa. As a result of chronic irritation from a stone long resident in the pelvis, granulomas may be observed in the pelvic mucosa.

Chronic infection in the ureteral mucosa, as in the pelvic mucosa, may produce similar lesions confined usually to one or two areas. Although rarely as generalized as ureteritis cystica, granulomas have, on occasion, been observed scattered over the entire ureter. When localized and occurring near the ureterovesical juncture, as in two of their cases, they closely simulate neoplasm. If a small stone is lodged in the intramural portion of the ureter, granulomas may be often seen protruding from the orifice into the bladder. Neoplasm is at once suggested, but in such cases the possibility of a small stone must be excluded.

Granulomas are usually associated with cystitis. Occasionally, many small areas of acute localized cystitis bearing minute granulomas are observed. The lesions are common in association with chronic cystitis; they may vary from one or two to several areas scattered over the entire bladder, and in these cases they are usually small, low, and without resemblance to neoplasm. This is particularly true of nonspecific cystitis.

The mucosa adjacent to the affected ureteral orifice is a frequent site of granuloma in renal tuberculosis. As this is also a common site of epithelioma, position is not of great diagnostic value. The distinction may be made from the fact that a granuloma will flatten out or largely disappear on full distention of the bladder, a phenomenon which will not occur in the presence of epithelioma. Further differen-

as clear celled without any other qualifying description are considered alone, it will be seen that a rather large proportion of his patients are in the group of those reported living.

A number of pathologists believe that the microscopic changes in renal tumors form a fairly accurate basis for an opinion as to prognosis.]

Gottlieb<sup>30</sup> stressed the importance of early and complete examination in cases of suspected renal tumor; such an examination to include urinalysis, cystoscopy, catheterization of ureters, chromocystoscopy, pyelography, pyelography aided by inflation of the renal pelvis, nephroscopy and pyeloscopy. Pyelograms are far more valuable than cystoscopic data. His operative cases have demonstrated the correctness and reliability of anatomic pictures as revealed by pyelograms, which permit a diagnosis of renal neoplasm, polycystic kidney or pelvic papilloma. When the kidney is small, pyelography, after abdominal inflation, gives excellent results. Gottlieb also called attention to the value of nephroscopy and pyeloscopy, a method of examining the patient before a screen in order to determine the dynamics of the kidney, its position, mobility and adherence to the adjacent organs. These data are of importance in determining whether operation can be performed in a given case. Hematuria did not prove to be an early sign in his cases.

Foged<sup>31</sup> reported a case of bilateral renal tumor in a child, aged 2 years, with a normal blood picture and without enlargement of the spleen or lymph nodes. After removal of the right kidney, typical lymphatic leukemia developed. Diffuse infiltration was found in the extirpated kidney. Foged considered bilateral renal tumor the first stage of aleukemic leukosis. His study of cases of renal tumor reported in the literature, in the material from necropsies of Copenhagen hospitals and of this case showed that leukemic disease of the kidney is seldom solitary, usually appears in typical leukosis, and most often in children. Only lymphatic leukosis was encountered. The infiltration is due to an increase in lymphocytes in the disturbed organ. The two kidneys are about equally affected. Macroscopically, the kidney seems hyperplastic; microscopically, universal infiltration without invasion of the renal epithelium is seen. The clinical picture is not characteristic. Foged stated that the bilateral nature of the lesion is an important diagnostic point.

*Granulomas.*—Braasch and Hurley<sup>32</sup> described granulomas found in the urinary tract as localized areas of hyperplasia of the mucosa and submucosa, apparently resulting from inflammation. These areas

30. Gottlieb, J.: Sur le diagnostic précoce des tumeurs rénales, *J. d'urol.* 24: 224, 1927.

31. Foged, J.: Leukemic Tumors of the Kidney, *Bibliot. f. Laeger.* 119:1, 1927.

32. Braasch, W. F., and Hurley, M. V.: Granulomas in the Urinary Tract, *J. Urol.* 18:595, 1927.



Gérard studied the different means of obtaining satisfactory roentgenographic shadows by the contrast method. He discussed colon insufflation, pneumoperitoneum, opaque ureteral catheters, pyelography and pyeloscopy. He used 30 per cent solutions of sodium iodide for pyeloscopy and 15 per cent for pyelography. Roentgen-ray examinations help in determining the situation, volume, shape, direction and extension of the surface of the kidney, the renal retention and the pelvic motility. In cases of lithiasis it permits precise treatment by indicating the site of the stone.

*Perirenal Hematoma.*—Meyer and Singer<sup>35</sup> showed that hemorrhage in the region of the kidney collects to form a localized hematoma. They showed that the differentiation of aneurysm of the renal artery and perirenal hematoma is clinically unsound. Conroy found thirty-four cases of aneurysm of the renal artery up to 1923, and Meyer and Singer have found six others. This does not include the cases of periarteritis nodosa, which are more common. Trauma, recent or remote in time and subcutaneous or perforative in type, was an etiologic factor in 50 per cent of these cases of aneurysm. Spontaneous rupture of the renal aneurysm may be due to atheromatous or calcific changes in a sclerotic vessel. In such cases, hypertension alone or hypertension and nephritis are present.

Renal arterial aneurysms are as a rule of the false variety. Periarteritis nodosa shows a predilection for the renal arteries and is characterized by a tendency to produce aneurysms. Syphilis, by producing gummatous arteritis, has been reported as a cause of perirenal hemorrhage. Emboli of the mycotic type may lead to miliary and larger aneurysms of the renal artery, which may subsequently rupture in a manner similar to that occurring in cerebral vessels as a complication of subacute bacterial endocarditis. Low grade suppuration of the renal pedicle appears to be responsible for erosion of the renal artery. In one of their cases, such an erosion led to sacculation and rupture. Jannsen described erosion and aneurysmal dilatation due to a sharp renal calculus. Seven days after the removal of the stone by nephrotomy, perforation of the renal artery occurred.

Conditions causing perirenal hematoma other than that due to renal aneurysms are considered; first there are the diseases of the parenchyma of the kidney such as tumors (hypernephromas, carcinomas, sarcomas and multiple cavernomas), tuberculosis, purulent processes, nephritis, nephrolithiasis, hydronephrosis and polycystic disease. In the latter, the presence of another factor must be considered, namely, abnormal fragility of the blood vessels or a blood dyscrasia.

Primary hemorrhage from the fibrous or fatty capsule of the kidney is next considered. This is comparable to hemorrhagic pachymeningitis

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35. Meyer, K. A., and Singer, H. A.: Spontaneous Perirenal Hematoma and Aneurism of the Renal Artery, *Surg. Gynec. Obst.* 45:300, 1927.



is not so much due to this fact as it is to a lack of appreciation of the three clinical syndromes for which they are responsible. Suprarenal dysfunction may be considered under the terms of hypochromaffinism and hyperchromaffinism as applied to the medulla, and hypo-interrenalism and hyperinterrenalism as applied to the cortex.

With respect to the cortex, hypofunction is exemplified by the clinical picture of Addison's disease. Hyperfunction of the cortex, occurring in either cortical hyperplasia or neoplasia, manifests itself clinically by characteristic alterations in the sexual sphere and by hypertension. The sexual changes are always toward the adult male type, irrespective of sex.

With respect to the suprarenal medulla, our knowledge of function is as yet too limited to serve as the basis for any known syndrome; yet the tumors of the medulla are in themselves so characteristic that little difficulty should be experienced in their diagnosis in most cases. The three clinical syndromes produced by suprarenal tumors may be considered under the following headings: cortical (carcinoma, or hyperplasia), (a) genitosuprarenal syndrome; medullary (neurocytoma, sarcoma), (a) Hutchison's syndrome and (b) Pepper's syndrome.

Cortical tumors are as common in infants and children as in adults, and are characterized by alterations in the sexual sphere, hypertension and, rarely, pigmentation. Medullary tumors belong distinctly to infancy. In both the Hutchison and the Pepper types the primary growth is generally masked by secondary manifestations; in the former, unilateral exophthalmos is frequently the first and only sign; in the latter, tremendous abdominal enlargement due to metastasis to the liver overshadows all else. These peculiarities render the prognosis in general extremely unfavorable, because the diagnosis, particularly in medullary tumors, is at present based wholly on metastatic phenomena.

Generally, a differential diagnosis of suprarenal tumors and other growths, as well as of cortical and medullary tumors of the gland itself, can be made by the clinical manifestations; yet the added information gained by urologic investigation is often of decided value.

Cortical tumors give rise to the so-called genitosuprarenal syndrome. The symptoms produced exemplify the endocrine activity of the cortex. In the female, sexual alterations are produced which may be expressed by the term "virilism" or "pseudohermaphroditism," and in the male by "precocious puberty." Hypertension is a frequent symptom of diagnostic value in these cases. Pigmentation, such as characterizes Addison's disease, is rarely seen. The Hutchison type of medullary tumor, occurring only in infancy and childhood, is characterized by early orbital metastasis producing unilateral exophthalmos. The primary

and is probably inflammatory in origin. It usually follows inflammations in the kidney or its pelvis. It is hemorrhagic perinephritis, and the hemorrhage may be intracapsular or extracapsular.

Morbid processes in retroperitoneal structures other than the kidney and its capsule, such as aneurysm of the abdominal aorta or the ovarian artery, tumors of the suprarenal gland or retroperitoneal tumors, such as angiosarcomas, may likewise lead to perirenal hematoma.

In hemophilia, hemorrhage may arise on rare occasions from the lumbar muscles, but the loss of blood by diapedesis may be alarming.

Diagnostically hematomas of the aneurysmal variety are associated with sudden pain (severe in type and situated in the region of the kidney), hematuria in 50 per cent of the cases, and tumor in the loin. On account of the small caliber of the renal artery, sacculation of it rarely reaches so considerable a size as to give expansive pulsation, thrill, and bruit, the pathognomonic signs of aneurysm. Peritoneal irritation is frequent; reflex vomiting and tympanites are more prominent features.

The symptoms associated with the nonaneurysmal varieties are severe pain, signs of internal hemorrhage, and a rapidly growing retroperitoneal tumor in the loin. Hematuria is rare in contradistinction to its frequency in the aneurysmal groups.

Vogeler reviewed twenty-nine cases up to 1922, and found that only five cases of aneurysm of the renal artery had been diagnosed before death. Likewise, the diagnosis of perirenal hematoma was made only three times up to 1921. The occurrence of severe pain, signs of internal hemorrhage and retroperitoneal tumor enlarging in the loin should suggest perirenal hematoma. Immediate operation is indicated in spite of an operative mortality of about 60 per cent, as conservatism is invariably fatal.

[Ed. NOTE.—This is a good review of a comparatively rare condition. As Meyer and Singer pointed out, the diagnosis before operation and death is rarely made by any one who has not had previous experience with a case in which the condition was undiagnosed until after death. The experience of Meyer and Singer with four cases has taught them to regard spontaneous perirenal hematoma as an entity demanding immediate surgical intervention. The symptoms of sudden severe pain in the region of the kidney, of signs of internal hemorrhage, and rapidly growing tumor in the loin should be emphasized as the features of a case which should bring this diagnosis up for consideration.]

#### SUPRARENAL GLANDS

*Suprarenal Tumors.*—Gibson<sup>36</sup> stated that tumors of the suprarenal glands are comparatively rare; yet the frequent failure to diagnose them

36. Gibson, T. E.: The Diagnosis of Adrenal Tumors with Classification of Adrenal Syndromes and Report of Cases, *J. Urol.* 18:33, 1927.

tumor. Bilateral pyelography was negative, as was surgical exploration of the right suprarenal gland. Permission for necropsy was not granted, so the diagnosis was not confirmed.

Crosbie and Smith<sup>37</sup> reported the case of a woman, aged 38, who had been normal until the age of 20 when an excess growth of hair appeared on the face and body. At 29, menstruation had ceased. Two weeks prior to admission to the hospital, fever, dysuria, frequency of urination and pyuria developed. A large tumor was found in the right flank. Pyelograms revealed a normal left kidney. The right kidney was on the left side of the median line and below the left kidney; its pelvis and calices pointed downward to the left.

The tumor was removed by operation and was found to be of the suprarenal, cortical cell type. Pyelograms made before the patient left the hospital showed that the right kidney had returned to its normal position with pelvis and calices facing the right side. Normal menstruation was resumed three weeks after the patient's dismissal from the hospital, after a period of nine years of amenorrhea.

The authors discussed the pathology of the suprarenal capsule, with special reference to the two major types of tumor, the medullary neuroblastoma and the cortical cell tumor, which may occur either as a benign adenoma or as a malignant true hypernephroma. The literature was carefully reviewed in detail and cases of other authors recorded.

This case seems to represent the nineteenth authentic case of cortical suprarenal tumor occurring in a female, with the typical changes in the secondary sex characteristics noted in relation to these tumors. It is apparently only the third or fourth case which has occurred in the adult during the child-bearing period, and also is one of the few cases on record in which the diagnosis has been confirmed by operation and a cure effected with reversion to the feminine habitus.

#### URETER

*Ureteral Stone.*—Jefferson<sup>38</sup> reported a ureteral stone that measured 83 by 41 mm. (3.25 by 1.63 inches) and weighed 106 Gm.

[ED. NOTE.—The stone reported by Jefferson is exceptionally large, especially since such conditions are now discovered in an early stage of the growth. In early reports of urinary calculi large stones were occasionally mentioned. Pozzi reported a stone weighing 34 Gm. and Fédoroff reported one of 52 Gm. The largest stone on record was reported by Carlls. This was in the pelvic ureter, and weighed 803 Gm.]

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37. Crosbie, A. H., and Smith, L. W.: Primary Tumors of the Suprarenal Capsule with Especial Reference to Adrenal Virilism, *J. Urol.* 19:241, 1928.

38. Jefferson, J. C.: A Large Ureteral Calculus, *Brit. M. J.* 1:14, 1928.

growth is usually small and the metastasis is generally the first sign of the disease. The Pepper type of medullary tumor is characterized by rapid abdominal enlargement due to metastasis to the liver. The primary growth is small and the hepatic metastasis is generally the earliest sign of the disease.

The diagnosis is ordinarily easy if these three pictures are remembered, and if the fact is also recognized that most abdominal tumors and enlargements in infants and children are due to either renal or suprarenal tumors. In adults, only 1 of every 200 tumors are renal in origin, whereas in infancy and childhood 1 of every 5 tumors are renal. Probably an even greater proportion are suprarenal in origin. Pyelography is of value in questionable cases.

The prognosis is extremely unfavorable, but the occasional cure following surgical intervention justifies this procedure. Urologic investigation to determine relative renal function is essential preliminary to operation, because it is necessary to remove a kidney with the tumor in a high percentage of cases. At operation, the opposite suprarenal gland should be palpated to determine its presence and whether or not the growth is bilateral.

Gibson, in an analysis of nine representative cases, gave concrete illustrations of the symptoms and diagnostic problems. In only four cases were suprarenal tumors found to be primary and of these one was a cortical tumor in a man aged 57. The systolic blood pressure was 190. The second case was that of a woman, aged 38, with a cortical tumor, who exhibited the typical sexual changes, bearded face, hairy chest, and hypertrophy of the clitoris. The third and fourth cases were both medullary tumors occurring in infants, one of the Hutchison type, the other of the Pepper type. The outcome was rapidly fatal in these four cases. Of the remaining five cases, three were secondary or metastatic growths in the suprarenal gland, and two were considered clinically as probable suprarenal tumors. In the three cases of metastasis, two were of the suprarenal glands, but symptoms pointing to suprarenal involvement were not present. In the third case, squamous cell carcinoma arising in the renal pelvis, had metastasized to the suprarenal glands. Typical symptoms of Addison's disease with pigmentation, asthenia, and low blood pressure characterized this case.

The two remaining cases were considered probable suprarenal tumors, but the diagnosis was not confirmed. One patient was a young man, aged 23, whose symptoms were obesity, marked hypertension, muscular weakness and a peculiar purplish discoloration of the skin. These symptoms were probably on the basis of either cortical hyperplasia or actual cortical tumor of the suprarenal gland. The remaining case was that of a female infant, aged 15 months, whose abdomen was large due to a large liver typical of the Pepper type of suprarenal

nephrosis. Diagnosis can be made cystoscopically if the tumor extends into the bladder. Occasionally particles of tumorous tissue can be dislodged with the ureteral catheter and recognized as a ureteral tumor. Stone, tuberculosis and ureteral stricture must be ruled out. If the ureteral catheter passes the area of the tumor, there may be a rapid flow of clear urine due to the release of retained urine; if there is also a tumor in the renal pelvis, the flow may be bloody. The ureterogram is the most useful diagnostic aid.

*Ureteral Diverticula.*—Rathbun<sup>41</sup> reviewed the literature of diverticula of the ureter and added two additional cases to those already noted by Stevens, and also reported one case of his own in detail, thus bringing the number to six cases. Rathbun's patient was a boy, aged 10, with a history of frequent urination since the age of 2. The urine was purulent. On cystoscopy, the ureteral orifices appeared normal, but ureteral catheters curled up in the diverticula just outside the wall of the bladder. A diagnosis of bilateral diverticula of the bladder with ureters opening into them was made. Later, at operation, the diverticula were shown to be of the ureters. The diverticula were excised and the ureters transplanted into the bladder with satisfactory results.

*Ureteral Trauma.*—Laurent<sup>42</sup> stated that the surgeon should be prepared to repair an injured ureter at any time. There are several types of operations in which ureteral injuries are not uncommon, such as hysterectomy for carcinoma of the cervix, the removal of tumors in the broad ligament and the freeing of inflammatory tumors of the adnexa. When the injury is noticed, an attempt should be made to restore the urinary route by an end-to-end anastomosis if the wound is high, or by vesical implantation if the injury is near the bladder.

There are several methods of caring for the injured ureter. Ureterorrhaphy and ureterocystoneostomy were practiced at one time but are now used only rarely, as the results are unsatisfactory. Ureteral implantation into the intestine following ureteral injury is now practically never done in France. Ureterostomy is indicated when both ureters are injured. Nephrectomy is occasionally performed. This precludes the possibility of later complications such as an ascending infection or hydronephrosis. Laurent favored ligation of the ureter; this is a simple procedure and is much less of a shock to the patient than a nephrectomy would be if an extensive gynecologic operation had already been performed.

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41. Rathbun, N. P.: Bilateral Diverticula of the Ureter: Case Report, *J. Urol.* 18:347, 1927.

42. Laurent, P.: De la conduite à tenir en présence des blessures de l'uretère au cours des interventions gynécologiques, *Paris chirurg.* 19:212, 1927.

*Ureteral Carcinoma.*—Carson<sup>39</sup> reported two cases of carcinoma of the prostate with metastasis to the ureter and also a case of primary carcinoma of the prostate with metastasis to the renal pelvis. There is a paucity of literature on this subject. Garceau reviewed thirteen cases of metastatic carcinoma in the ureter due to extension by continuity. Giordano and Bumpus reported a case of carcinoma of the left ureter and renal pelvis which did not show invasion of the lymphatics of the ureter, but they were able to demonstrate cancer cells in the blood vessels of the lungs and in a metastatic renal infarct, and thus to conclude that transmission occurred by way of the blood stream. Thomas and Regnier, in 1924, likewise reported a case of carcinoma of the bladder with metastasis to the lymph nodes, psoas muscle and right ureter, without indicating the path of transmission.

Carson's two cases and those previously reported were noted at necropsy, the patients having died of carcinoma of the prostate. At necropsy, the lymphatics of the ureter were found invaded by cancer cells, the growth involving the ureteral walls.

The lymphatics of the ureter are more numerous in the adventitia and muscular coats. They accompany the arteries and drain in three directions, the lower portion downward in the direction of the bladder, the pelvic and abdominal portions mesially into the pelvic and lumbar lymph nodes, and the upper portion in the direction of the renal lymphatics. Thus, while the lymphatic system is doubtless the earliest and most frequent site of metastatic lesions in carcinoma of the prostate, it seems that the drainage of the lymph downward in the lower portion of the ureter is the explanation of the rarity of metastasis to the ureters from the prostate or other pelvic viscera.

[ED. NOTE.—Carcinoma of the cervix and prostate by local infiltration may sometimes cause pressure on the ureter, but, as this study shows, direct lymphatic transmission of the disease to the ureter is not the rule. Carson's cases may present a phase of retrograde extension of malignancy against the lymph stream which may be confusing in the consideration of carcinoma in other organs.]

Key and Akerlund<sup>40</sup> referred to the importance of roentgen-ray examination in the diagnosis of rare ureteral tumors. These are either primary or secondary to renal tumors and are usually epithelial. Fifty-four such cases have been reported by Stewart, and to these Key and Akerlund added two. Symptoms are not characteristic, but with the aid of the roentgen ray many cases can be diagnosed. The usual sign is hematuria, and in 55 per cent of the cases hydronephrosis or hemato-

39. Carson, W. J.: Metastatic Carcinoma in the Ureter: Report of Additional Cases, *Ann. Surg.* 86:549, 1927.

40. Key, E., and Akerlund, A.: Ueber die Diagnose der Uretertumoren, *Deutsche Ztschr. f. Chir.* 200:428, 1927.



Thus the field of pancreatic efficiency tests is, at the present time, limited to a few pathologic conditions and cannot be used as a general routine procedure to differentiate pancreatic lesions from other abdominal conditions.

It is possible that with the culmination of the present work being done on secretin, a satisfactory method can be devised through the estimation of complete activity by specific stimulation and its quantitative estimation through the medium of fecal amylase determinations. With the present methods, the only conclusion that can be drawn from a pancreatic function test is whether or not the pancreas is able to produce sufficient enzyme for normal digestive function, or that there be obstruction to the duct.

#### METHODS FOR DETERMINING PANCREATIC FUNCTION

Many tests have been devised, but none have been successful to a satisfactory degree. For purposes of discussion a number of them are cited.

*Dye Tests.*—Giichiro tested nine dyes for selective pancreatic secretion, using dogs with Pawlow fistulas. Methylene blue (methylene chloride, U. S. P.) was secreted in small amounts.

Ivy tried thirty-three dyes, with the result that the pancreas was shown to secrete minute quantities of methylene blue and methyl violet, but not sufficient amounts to be used for quantitative estimation.

*Miscellaneous Tests.*—Decker used Loewi's test in 500 miscellaneous cases without conclusive results.

Cockcroft used Loewi's epinephrine mydriasis test in two significant cases: 1. A case in which a normal pancreas was found at autopsy gave three negative tests on separate occasions. 2. A case in which the pancreas was found to be almost completely disorganized from malignancy, gave marked positive reactions, the last test being made three days before death. These cases serve to illustrate the absolute inaccuracy of the test.

Lutz expressed the belief that the Bassler test is of great diagnostic and prognostic value, but there is not sufficient evidence to warrant such conclusions. Bassler and Lutz presented a series of ten cases with various degrees of involvement of the gallbladder and pancreas. They claimed to have demonstrated the specificity of the test, but the results are not convincing.

Schmidt devised a test using nuclear digestion as an index. This test shows relatively little, as it is purely qualitative.

Goetz believed that the von Ehrman test is more reliable than determinations of the blood and urine diastase. He believed that the method will show deviations from the normal. The evidence is not conclusive.

## PANCREATIC FUNCTION TESTS

WITH SPECIAL REFERENCE TO THE QUANTITATIVE DETERMINATION  
OF FECAL AMYLASE \*

JOHN A. WOLFER, M.D.

Associate Professor of Surgery, Northwestern University Medical School  
CHICAGO

AND

L. W. CHRISTIAN, B.S.

DETROIT

At the present time, there are no adequate means of estimating pancreatic function. Many tests have been devised and modified, but sooner or later have been discarded. The chief objection seems to be that clinical diagnoses cannot be confirmed by such tests with any reasonable degree of accuracy.

That several of the present means of estimation are based on sound principles is evident, but entirely too much has been expected of the tests. With the present means, diseases of the pancreas of a mild degree, or relatively nondestructive, cannot be determined.

The probability that the pancreatic tissue is normally present in an amount far in excess of the actual enzyme requirement seems to have been overlooked or disregarded in much of the work that has been done. Criticism that has been offered in connection with the problem has not taken this factor into consideration. It seems likely that the pancreas, as well as other secretory organs, normally secretes amounts in proportion to the needs of the body, and one may as logically assume that a disease process would have to involve a considerable portion of the gland before it would fail to supply the amount of enzyme necessary for digestion. Therefore, any test aimed at the determination of pancreatic hypofunction would show only positive results if sufficient gland substance was involved to overcome the large amount of secreting cells present as a "safety factor," and enough more to cause an actual reduction below the necessary amount.

With this idea in view, it cannot be said that pancreatic function tests being normal, the pancreas is not diseased; only in case there is obstruction to the outflow of digestive enzymes would there be increased diastase in the blood or urine or decreased diastase in the feces or duodenal contents without a considerable portion of the gland being diseased.

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\* From the department of Surgery and the Laboratory of Surgical Research, Northwestern University Medical School.

series of ten patients was used in his determinations. His results, however, are not conclusive.

Moller determined urinary diastase in twenty-three cases in which there was tenderness in the region of the pancreas. He found the diastase present in unusual amounts. Eight cases were proved at operation to be pancreatic disease, but he does not say to what extent the pancreas was found involved.

Markowitz and Hough have shown that after pancreatectomy in dogs the blood diastase is at first increased and then falls to below the highest normal level within twenty hours. They did not see any justification for determinations of the blood diastase in diabetes mellitus.

*Diastase in Feccs.*—Wohlgemuth (1910) gave the average normal value for amylase in feces as  $Df \frac{38^\circ}{24h} = 468.75$ . The lowest normal values are 100. In one case of obstruction of the pancreatic duct, he reported a fecal amylase of 15.

McClure and Pratt (1917) showed that in obstruction to pancreatic secretion in man and dog there is marked diminution or absence of diastatic activity in feces. They believed, however, that the estimation of fecal amylase is of little value in the clinical diagnosis of pancreatic disease.

*Comment.*—Dye tests and such miscellaneous tests as have been cited have not proved satisfactory, and results in the hands of others than the original investigators have shown nothing of importance.

Determinations of blood and urine amylase will not show evidence of pathologic process except in obstruction to the outflow of pancreatic secretion. Even then the effect is transitory, as shown by Markowitz and Hough. There is no sound physiologic reason for this determination in other than obstructive cases.

In the estimation of diastase in the duodenal contents, the work of McClure and his associates has been successful to a certain extent. Their work shows that it is only by causing a stimulation to pancreatic secretion and the determination of complete functional capacity that an accurate idea of the state of the pancreas can be determined. Their tests, however, are not satisfactory. Grote has shown that the duodenal tube cannot be relied on to collect uniform samples in all cases. Further, they have not used a specific stimulus, and the test has not shown uniform results in other hands.

Ivy and Koskowski (1926) have shown that there is no compensatory amylase secretion by the succus entericus following pancreatectomy. Wohlgemuth and McClure have both shown that determinations of fecal amylase are of value in determining obstruction to the outflow of pancreatic secretion. Work on other phases of the test has not been done; hence its use in the present work.

Wallis completed an investigation of pancreatic function tests.. He reported unfavorable results with an oil test meal (trypsin and diastase determination), Sahli's test, Cammidge test, Koshwadis modification of the Schmidt test and the Sajodin test of Winternitz. He believed that a positive Loewi's test together with diastase in the urine and glycosuria would be a valuable indication. He did not believe that the others were of value.

*Estimation of Diastase in Duodenal Contents.*—Buckstein (1922) modified the Einhorn test (1912) by using a celluloid capsule attached to a thread which he passed into the duodenum. He reported favorable results, giving the normal value as from 3 to 7 units. Further evidence could not be found to support his method.

Gavrila and Paraschivesco used the method of Einhorn in eleven cases of diabetes mellitus. They believe that the results will not show a parallel with the severity of the diabetes, and, therefore, that it is of little value in this disease.

De Loch modified Einhorn's method, using .30 cc. of tenth normal hydrochloric acid as a stimulus. His claims are too great for the amount of evidence presented.

Whipple minimized the value of the duodenal tube method of determination of enzymes. Grote claimed that the duodenal tube methods are not of value because: 1. The secretion varies in different parts of the duodenum. 2. Ether is not a reliable artificial stimulus. 3. The reaction varies the enzyme activity. 4. Variation of the results in normal persons is too great. Grote expressed the belief that the best way to determine pancreatic function is by a test meal and examination of the stool.

Labbe, Nepveux and Adlersburg (1925) modified the Katch method of injection of ether through the duodenal tube. They gave magnesium sulphate first to evacuate the gallbladder, and then ether to stimulate the pancreas. They reported favorable results in three of seven cases.

McClure, Jones, Wetmore and Reynolds (1924) claimed to have established the normal pancreatic enzyme concentration of the duodenal contents. They claimed to show diminution of the enzyme in obstruction and concentration of it in necrosis of the pancreas. Their method seems to be safe in their hands, but unreliable with others.

*Determination of Blood and Urine Diastase.*—Permin (1924) gave the normal urine diastase value as from 8 to 16 units and reported a case of suppurative cyst of the pancreas with a urinary diastase of 1,024 units. He said that massage of the pancreas and artificial pancreatitis will produce elevated urinary diastase in rabbits.

Von Strasser (1926) gave the figures for normal blood diastase as from 8 to 16 units. He said that any value over 32 is pathologic. A

increases its activity 4.5 times. Acid of above 0.009 per cent hydrochloric acid inhibits the action of amylase, as does 0.04 per cent lactic acid.

*Sedimentation.*—The results are in terms of solid fecal sediment to eliminate the bulk of the error that would result from perverted water content due to diarrhea or constipation. This is believed to be better than the old method of desiccation which tends to deteriorate the enzyme.

Acid reaction was checked by titration with tenth normal sodium hydroxide.

*Fecal Amylase Determination in Normal Persons.*—Since Wohlge-muth's values are dogmatic and do not show whether there is or is not a definite normal variation in diastase content of the feces, it was deter-

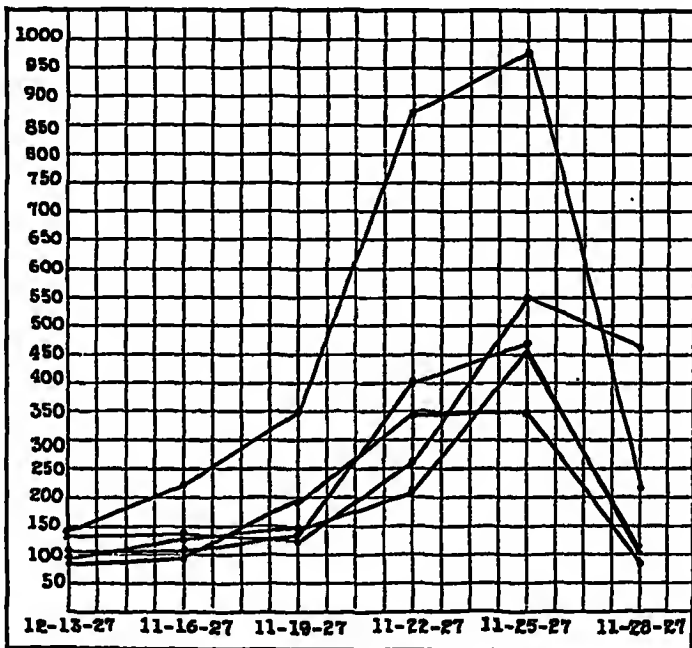


Chart 1.—A graph of the fecal amylase values of normal persons, taken every third day. The values are in terms of  $Df_{24\ h}^{38^\circ}$ .  $Df_{24\ h}^{38^\circ}$  = cc. of 1 per cent starch solution digested by the amylase in 1 cc. of centrifugalized fecal sediment at 38 C. in twenty-four hours. This chart shows a definite parallel in the rise and fall of the curves.

mined expedient to run a series of controls. For this purpose medical students, two groups of five each, were selected. These men ate their meals at the same fraternity house table, and, with the exception of candy, peanuts, etc., the diet was essentially the same.

Series 1: Five men, under the conditions already described, participated in this series. The stools were examined for diastase content every third day for eighteen days (chart 1). The results are shown in table 1.

It can be seen from the graph in chart 1 that while there is some slight variation, the diastase seems to vary as the diet and in the same

It is probable that with the advent of secretin in a purified form, we may be able by its administration to secure complete stimulation to the pancreas and by the determination of amylase in the feces, secure a definite quantitative estimation of the functional capacity of the pancreas. This work awaits a purified nontoxic secretin of known specific action.

#### FECAL AMYLASE DETERMINATIONS

Amylase is chosen in preference to either of the other two pancreatic enzymes, because: 1. With it the reversibility of the hydrolytic reaction is negligible (Hollander and Marcus—1925). 2. The time law of Hedin can therefore be applied to this reaction. 3. Kjeldahl's law of proportionality may also be applied to diastase (Sherman and Kendall—1910). 4. The enzyme is less effected by outside influences than are lipase and trypsinogen. The feces were used as a source for the amylase in preference to blood, urine or duodenal contents, for these have not proved to be satisfactory, as shown by the review of the literature.

*Method.*—Hawk (1927) modified the Wohlgemuth test and his modification was used in these determinations. The test is based on the extraction of amylase from fresh feces by a phosphate-chloride buffer solution and the digestion of it in varying amounts against 5 cc. of 1 per cent soluble starch. The digestion is carried out in an incubator at 38 C. for twenty-four hours, and the end-result is determined by the starch-iodine reaction. Details of the technic are given in Hawk's "Physiological Chemistry" (1927).

Twenty-four hours was used in preference to shorter periods for digestive action, for it has been shown that 1 C. variation in temperature will throw the results off 10 per cent when only one-half hour is allowed for digestion (Sherman, Kendall and Clark—1910). The starch-iodine reaction was used in preference to the more careful copper reduction reactions, for while it is not so delicate, it is simple, practical and as accurate as the clinical results warrant. It has the advantage of marking the completion of a fairly definite step in the digestion of starch, whereas the copper reduction method measures the amount of substance or substances produced by successive steps through intermediate products which are but imperfectly known (Sherman, Kendall and Clark—1910).

*Phosphate-Chloride Buffer.*—Hawk (1911) has modified Wohlgemuth's original method by adding phosphate-chloride buffer solution to the reaction as a diluting medium. Sherman and Kendall (1910) and Hawk (1911) have shown that amylase is not completely activated unless electrolytes are present.

Vernon (1901-1902) and Chittenden and Griswold (1881) have shown that a trace of acid—0.004 per cent hydrochloric acid markedly (four times) activates the enzyme and that lactic acid 0.0083 per cent

rather than because of pancreatic deficiency. This factor must be taken into account in evaluating clinical results.

5. It is reasonable to believe that this test used clinically can become effective only if the patients are placed on a uniform, quantitative and qualitative diet.

Series 3: A third series of five students was used under conditions similar to those in series 1 and 2, except that the total stool was saved for each twenty-four hours for seven consecutive days.

Determinations of amylase in twenty-four samples necessitated a slight modification of the previously described technic, as follows:

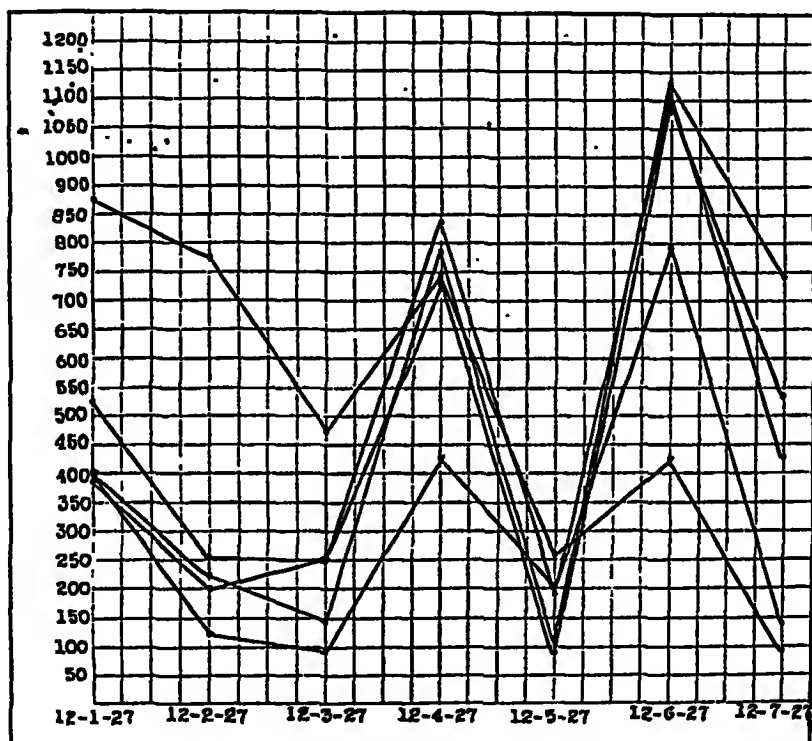


Chart 2.—A graph of the fecal amylase values of normal persons, showing weekly variation. The values are in term of  $Df \frac{38^\circ}{24\text{ h}}$ . This chart also shows a distinct parallel in the rise and fall of the curves.

1. The twenty-four hour stool specimen was placed in a 1.5 liter granite bowl, and sufficient phosphate-chloride buffer solution was added to make 500 cc.

2. The mixture was thoroughly stirred, any mechanical contrivance at hand being used, such as a pestle, egg-beater or anything which would aid in securing a mixture of uniform consistency.

3. The mixture was allowed to digest for one-half hour, being stirred occasionally.

person may cover a wide range of values, depending on the food intake. As the direction of variation is parallel in practically all cases, we may assume that a given diet has practically the same stimulating effect on the pancreas in all normal persons. None of the values as shown in table 1 fell below the value of  $Df. \frac{38^{\circ}}{24h} = 91$ . It is conceivable that a healthy person receiving an average diet should not have a normal value below 90, which value is ten points below the lowest normal value as determined by Wohlgemuth.

Series 2: Another group of five medical students participated in this series under the same conditions as those in series 1. Fecal amylase was determined daily for one week, to show the day to day variation (chart 2). The results are shown in table 2.

TABLE 1.—Data on Series 1\*

Patient	Nov. 13	Nov. 16	Nov. 19	Nov. 22	Nov. 25	Nov. 28	Average
G. ....	145	226	350	870	981	222	466
D. ....	99	128	133	210	476	110	192
M. ....	91	97	180	342	345	162	193
R. ....	101	102	127	400	400	96	216
B. ....	143	131	120	204	547	461	277

\* The foregoing values are in terms of  $Df. \frac{38^{\circ}}{24h}$ . A graph of these figures is shown in chart 1.

TABLE 2.—Data on Series 2\*

Patient	Dec. 1	Dec. 2	Dec. 3	Dec. 4	Dec. 5	Dec. 6	Dec. 7	Average
W. ....	400	125	91	423	190	793	91	302
C. ....	871	782	473	732	237	470	108	537
T. ....	400	221	143	778	118	1,130	472	504
B. ....	386	200	250	732	91	1,087	530	468
R. ....	520	200	250	836	200	1,110	420	513

\* The values in this table are in the same terms as those in table 1.

Again it will be seen that a close parallel exists between the values, although the variation from day to day in the same person occurs through a wide range. Again we assume that the main factor in this variation is diet.

From this series, the following conclusions were made: 1. The amylase output of the pancreas varies from day to day, depending largely on the intake of food.

2. The value for persons on the same diet is relatively the same on the same day.

3. The normal average varies from 302 to 537, with  $Df. \frac{38^{\circ}}{24h} = 465$  as the normal average. This value is close to that set by Wohlgemuth (468.75).

4. It is logical to assume that persons with various degrees of pancreatic disease might show low values because of low food intake



Isaacs and Kreiger studied thirty cases of achlorhydia and did not find abnormality in diastase. They concluded that there were normal diastase values in cases of "gastrogenous diarrhea."

McClure, Jones, Wetmore and Reynolds (1924), from a study of diastase in duodenal contents, concluded:

1. Chronic pancreatitis shows depressed diastase values.

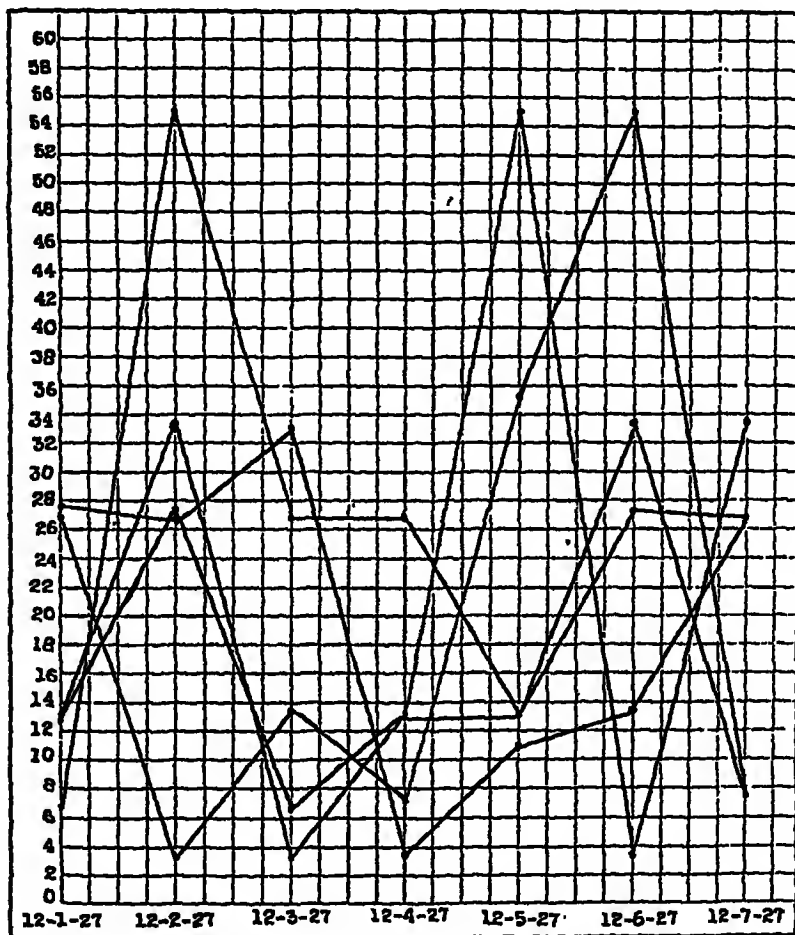


Chart 3.—A graph of the total fecal amylase in twenty-four hour specimens from normal persons, the determinations being made on seven consecutive days. The values are in terms of liters of 1 per cent starch solution digested by the amylase in the twenty-four hour specimen of stools. This chart shows the marked variations in the amount of amylase in the twenty-four hour specimens either of persons on the same diet or of the same persons from day to day. There is not a suggestion of a parallel in the curves.

2. Acute pancreatic necrosis and carcinoma of the pancreas show abnormal (?) values.

3. Obstruction to the outflow of pancreatic enzyme shows diminished or absent values.

4. Necrosis shows concentration of the enzyme.

4. A 15 cc. representative portion was measured out and placed in a graduated centrifuge tube and centrifugalized for fifteen minutes.

5. From this point, the technic was the same as that of the Wohlge-muth-Hawk method already described, except that the final reading was in terms of the amount of standard 1 per cent starch solution—in liters—that will be digested by all the amylase in the twenty-four hour specimen.

The results are shown in table 3 and chart 3.

From table 3 and chart 3, it can be seen that there is no constant relation between the amount of amylase in twenty-four hour specimens, either of persons on the same diet or of the same person from day to day, although the weekly totals approximate each other rather closely.

It seems logical to conclude that the motility of the gut affects the total twenty-four hour output, and that there is a wide margin of individual variation due to innumerable factors. From the previous series, it does not seem that gastric motility affects the amount of amylase in any

TABLE 3.—Data on Series 3

Patient	Dec. 1	Dec. 2	Dec. 3	Dec. 4	Dec. 5	Dec. 6	Dec. 7	Total Output
W. ....	26.80	3.3	13.00	6.65	53.3	55.0	6.65	144.40
O. ....	6.65	55.0	26.80	26.80	13.3	27.3	26.80	182.65
T. ....	13.30	33.3	3.30	13.30	55.0	3.3	33.00	154.50
B. ....	12.80	27.3	6.65	13.30	13.3	33.3	6.65	113.50
R. ....	27.80	26.8	33.00	3.30	12.8	13.3	26.80	143.50

The results in this table are in terms of liters of standard starch solution (1 per cent) which will be digested by all the amylase in the twenty-four specimen.

one average selected portion of stool of persons on the same diet at the same time. It seems most likely that the amylase present in a unit volume varies as the food intake and not with gastric motility, the values being in terms of solid fecal sediment. It is probable that equal portions of the same kind of food will stimulate the pancreas to secrete a definite amount of amylase in all normal persons and that its mixture with that portion of food will be relatively the same concentration, the factor of water dilution being removed.

#### CLINICAL INVESTIGATION

*Previous Work.*—Considerable work has been done on the determination of pancreatic enzymes as an index to pancreatic disease. A few examples have been selected from the literature.

Wallis (1920), from a study of eight cases of acute pancreatitis, twenty-eight cases of chronic pancreatitis, five cases of carcinoma of the head of the pancreas, twenty cases of disease of the liver and thirteen miscellaneous cases, concluded that he could diagnose pancreatic disease if Loewi's test, glycosuria and increased diastase in the urine all showed positive results. Confirmation of his work was not found.

Gavrila and Paraschivesco (1926), using the method of Einhorn, analyzed eleven cases of varying degrees of diabetes mellitus and concluded that the diminution of pancreatic secretion is not parallel to the severity of the diabetes.

Landan, Cygielstrejck and Fejgin (1926) found four cases of achylia gastrica associated with "pancreatic achylia." The patients had pernicious anemia, and the authors suggested that the pathologic process in these two organs may be part of the clinical picture of the disease.

Silverman (1927), determining duodenal diastase, concluded that sprue shows normal pancreatic ferments. Manson-Bahr demonstrated histologically for him that the histologic structure of the pancreas was normal in this disease.

*Clinical Cases.*—Determinations of fecal amylase were made in a series of cases including four cases of known chronic pancreatitis, proved at operation; five cases of chronic cholecystitis with stone, proved at operation; two cases of chronic cholecystitis with stone, not proved by operation but clinically positive; two cases of chronic cholecystitis-noncalculus, proved at operation; three cases of chronic cholecystitis, not operated on but clinically positive; one case of stone in the common duct in which the gallbladder had previously been removed, not proved at operation but clinically positive; and five miscellaneous cases.

These patients were placed for twenty-four hours on a fixed diet, as follows:

*Breakfast:*

Dish of oatmeal (about two-thirds cupful)  
Toasted white bread (one slice)  
Whole milk (8 ounces)

*Dinner:*

Buttered white bread (one slice)  
Whole milk (8 ounces)  
Lean steak (6 ounces)  
Boiled potato (1 medium sized)  
Corn starch pudding (two-thirds cupful)

*Supper:*

Toasted white bread (one slice)  
Whole milk (8 ounces)  
One poached egg  
Corn starch pudding (two-thirds cupful)

The first stool specimen, passed twenty-four hours after the last meal of the diet, was saved and the fecal amylase determined after the method of Wohlgemuth-Hawk, as in series one and two of the normals.

Although many of the foregoing values are below the lowest values (91) found in the normal series, operation confirmed gross changes in

McClure, Montague and Mortimer (1924), also McClure, Jones and Chester (1922) concluded that patients with achylia gastrica have normal pancreatic function as determined by diastase in the duodenal contents.

Labbe, Nepveux and Adlersburg (1925), from a study of duodenal content diastase, concluded that:

1. Diastase was decreased in patients with cholelithiasis as well as in destructive lesions of the pancreas.

TABLE 4.—*Data on Fecal Amylase Determinations in Clinical Cases*

No.	Patient	Age	Disease	38° Df. —	Sex
				24 h.	
1	O. K.	68	Chronic cholecystitis with stone, proved.....	335.0	F
2	M. S.	34	Chronic cholecystitis with stone, proved.....	57.1	F
3	C. P.	25	Chronic cholecystitis with stone, proved.....	107.0	M
4	M. L.	43	Chronic cholecystitis with stone, proved (with pancreat- itis) .....	240-201	F
5	E. K.	48	Chronic cholecystitis with stone, proved (stone in am- pulla with obstructive jaundice).....	52.6	F
6	S. M.	46	Chronic cholecystitis with stone, not proved.....	71.1	M
7	D. S.	36	Chronic cholecystitis with stone, x-ray positive.....	100.0	F
8	E. L.	28	Common duct stone, not proved.....	322.0	F
9	E. E.	50	Chronic cholecystitis, proved (diffuse sclerosis of pan- creas) .....	60.0	F
10	O. K.	..	Chronic cholecystitis, proved.....	238.0	F
11	I. W.	..	Chronic cholecystitis, not proved.....	62.4-62.5	F
12	J. K.	24	Chronic cholecystitis, not proved.....	92.5-36.9	M
13	M. E.	..	Chronic cholecystitis, not proved.....	22 -26.3	M
14	J. N.*	36	Chronic diffuse pancreatitis, with obstruction.....	16.8	M
15	S. S.	38	Chronic diffuse pancreatitis.....	23.0	F
16	M. C.	58	Carcinoma of head of pancreas.....	100.0	F
17	F. D.	43	Chronic nonulcerative colitis.....	62.5	M
18	J. H.	34	Chronic nonulcerative colitis.....	335.4	M
19	C. S.	32	Chronic nonulcerative colitis.....	57.1-117.6	M
20	J. G.	41	Sprue .....	100-103.7	M
21	M. H.	38	Acute yellow atrophy of liver.....	62.5	F

\* Case 14 (J. N.) came to autopsy on July 10, 1928. The right one third of the pancreas was replaced by carcinoma, the middle third contained little normal gland tissue and consisted essentially of carcinoma. The left third was extensively infiltrated by connective tissue with marked diminution of gland tissue. The duct was virtually obstructed by a carcinomatous nodule growing into the ampulla of Vater. A fine probe could be forced through the opening. The duct of Santorini was obliterated. The pathologist's opinion was that 90 per cent of the gland had been destroyed. The low fecal amylase values are therefore significant.

2. They also found decreased diastase in three of seven patients with diabetes mellitus.

Bassler and Lutz (1925), using Bassler's test, analyzed ten cases and concluded:

1. Chronic cholecystitis, especially with stone, shows a low value (from 2 to 7 units).

2. One case of carcinoma of the gallbladder and pancreas showed a negative test.

Cockcroft (1920), in direct contradistinction to Bassler and Lutz, using the same tests, found destructive lesions showing a positive reaction, while a case in which the pancreas was normal showed a negative test several times.

thought that the cases of colitis might show an excess of acid in the stools and thus inhibit amylitic activity (Vernon), but amylase determined with the buffer solution as the diluting medium showed practically normal reactions. The Vernon theory of acid inhibition cannot here be displayed, for an excess of acid was not present.

In the case of sprue (case 4, J. G.) there was no decrease in fecal amylase value (100 and 103.7), which confirms the conclusion of Silverman.

In the case of acute yellow atrophy of the liver with changes in all the abdominal organs (determined at autopsy three days after the test), a value of 62.5 was found, which is below the lowest normal value—91. This may have been due to destructive changes in the pancreas, with actual decrease in the necessary amount of secreting tissue.

*Conclusions.*—1. Cases of obstruction to the duct will show a decrease in fecal amylase (confirmed by McClure).

2. Cases in which there is diffuse involvement of the pancreas, such that it cannot supply sufficient amylase for normal digestive processes, will show decreased fecal amylase.<sup>1</sup>

3. At the present time, cases with mild involvement of the pancreas cannot be confirmed by determinations of fecal amylase, probably owing to the "safety factor" of secreting tissue normally present.

4. It may be that with larger series of cases of carefully conducted clinical experiments, the same diet being used in all cases, we may be able to demonstrate cases with mild involvement of the pancreas.

#### f ANIMAL EXPERIMENTS

Four dogs were prepared as follows: A short loop of bowel, from 15 to 20 inches (37.5 to 50.8 cm.) from the tail of the pancreas, was transplanted underneath the skin of the abdominal wall, just lateral to the umbilicus. Several days later, a fistula was made into this loop. The dogs so prepared were used as follows:

*Dog 1.*—This animal was fed a daily meal of 800 cc. of meal mash and 300 Gm. of bread. Three times weekly, beginning fifteen minutes after the meal was eaten, 10 per cent sodium bicarbonate solution was allowed to perfuse through the bowel by means of a gravity bottle and dropping tube which was connected by a catheter (no. 14 F.) passed into the distal portion of the transplanted loop such that 500 cc. will pass through in one hour. Fecal amylase determinations were done on the two specimens of feces passed following such perfusion. Results are shown in table 6.

1. A case of hyperinsulinism due to a carcinoma of the pancreas metastasizing into the liver is now under study. Fecal amylase values are from 110 to 80; the total for the twenty-four hour specimen is 6.65. The blood sugar at the time of amylase determinations was 0.049. This patient does not exhibit any signs of obstruction of the duct and no doubt the pancreatic "safety factor" is encroached on at the present time, as an amylase value of 80 is below our normal standard.

the pancreas in only three cases. Lack of operation in several cases deprived us of confirmative evidence. We cannot, therefore, say that values below 91 are indicative of pancreatic disease. E. K. (case 5) had a stone in the ampulla of Vater and J. N. (case 14) a diffuse pancreatitis with obstruction of the duct, each with jaundice, and the low amylase values were probably due to obstruction to the outflow of pancreatic juice, although in case 14 there was an extensive change in the pancreas.

The case of carcinoma of the head of the pancreas (M. C.) shows the lowest normal level, and it is likely that an insufficient amount of pancreatic tissue was involved to decrease the amount of secretory cells below the actual dietary requirements. In this case, there was no evidence of obstruction of the duct.

TABLE 5.—*Dextrose Tolerance Test in Cases 4 and 9*

<b>Case 4</b>		
Fasting sugar.....	140	Urine sugar negative
First hour.....	153	Urine sugar plus with 15 drops
Second hour.....	151	Urine sugar two plus with 15 drops
Third hour.....	148	Urine sugar plus with 15 drops
Fourth hour.....	...	Urine sugar negative
<b>Case 9. Before cholecystectomy</b>		
Fasting blood sugar.....	96.0	Urine sugar negative
First hour.....	164.0	Urine sugar negative
Second hour.....	164.0	Urine sugar, trace
Third hour.....	127.5	Urine sugar negative
<b>161 days after cholecystectomy</b>		
Fasting blood sugar.....	93.0	Urine sugar negative
First hour.....	201.0	Urine sugar, 0.17 per cent
Second hour.....	209.4	Urine sugar, 7.1 per cent
Third hour.....	243.0	Urine sugar, 5.6 per cent

Of the three cases of proved nonobstructive pancreatitis, all of long duration, two showed values considerably below the lowest normal level (20 and 60). There was much more extensive involvement of the pancreas in these two than in the third (case 4, M. L.), in which the process was mostly confined to the head of the organ, and in which the values were well within the normal (246 and 201). Dextrose tolerance determinations were made in these cases with the result that the tests would further indicate that the secretion of the pancreas is diminished more in cases 9 and 15 than in 4.

In case 15, the patient had active diabetes, so a sugar tolerance test was not attempted.

The case of limited pancreatic involvement seems to demonstrate that unless the changes in the pancreas are marked, it will secrete, under normal stimulus, sufficient enzyme to digest normal food intake. The results of Brown parallel these observations.

In the three cases of chronic nonulcerative colitis showing varying degrees of amylitic activity, conclusions cannot be drawn. It was

Farrell and Ivy have shown in dogs with pancreatic transplants and Thiry fistulas that:

1. Administration of 150 cc. of tenth normal hydrochloric acid markedly stimulated the pancreatic secretion.
2. One hundred and fifty cubic centimeters of water or 0.3 per cent sodium carbonate stimulated secretion but to a milder degree, the carbonate being less active than water.

Our results on experimental work done show:

TABLE 8.—*Data on Dog 3*

Date	Cc. of 1.25% Lactic Acid	First Specimen	Amylase Df ——— 38 ° 24 h		Control
			Second Specimen		
5/ 2.....	...	....	.....		581
5/ 5.....	100	1,032	3,276		...
5/ 7.....	150	976	4,800		...
5/ 9.....	150	1,248	5,569		...
5/12.....	200	630	5,827		...
5/14.....	250	460	6,410*		...

\* This value may have been higher as it was the last tube in the series.

TABLE 9.—*Data on Dog 4*

Date	Cc. of 1.25% Lactic Acid	First Specimen	Amylase Df ——— 38 ° 24 h		Control
			Second Specimen		
5/14.....	...	....	.....		370
5/16.....	100	....	2,710		...
5/19.....	150	1,510	3,276		...
5/21.....	150	1,712	2,634		...
5/21.....	150	1,248	4,896		...
5/23.....	200	....	5,569		...
5/24.....	200	1,032	5,569		...
5/25.....	250	976	5,827		...

1. The administration of 1.25 per cent lactic acid (from 100 to 250 cc.) through a jejunal fistula markedly stimulates pancreatic secretion, and the stimulation is progressively greater as the amount given increases. Such increases can be demonstrated by the quantitative determination of fecal amylase.

2. The administration of 10 per cent sodium bicarbonate solution (from 100 to 400 cc.) markedly stimulated the secretion of the pancreas although to a lesser degree than does 1.25 per cent lactic acid. This increased secretion can also be demonstrated by fecal amylase determinations.

*Dog 2.*—This animal was fed the same as dog 1. The perfusion was done in the evening from about eight to ten hours after the ingestion of the meal. The results are shown in table 7.

In the case of each dog, it was found that in amounts up to 150 cc., the alkaline perfusion was well tolerated. If greater amounts than this were used, the dog salivated, became nauseated and vomited from 10 to 20 cc. of the meal. In the case of dog 2, which was given the perfusion several hours after the meal, nausea was present after 150 cc., but the dog did not regurgitate although reverse gastric peristalsis seemed to be present at intervals.

TABLE 6.—Data on Dog 1

Date	Cc. of 10% NaHCO <sub>3</sub>	First Specimen	Amylase Df		Control
			38 ° 24 h		
3/26.....	...	...	.....		444
3/31.....	100	782	1,540		...
4/ 1.....	...	...	.....		230
4/ 2.....	150	471	1,620		...
4/ 4.....	150	160	1,810		...
4/ 7.....	200	812	2,034		...
4/ 8.....	...	...	.....		264
4/ 9.....	250	1,026	1,760		...
4/11.....	...	.....	.....		194
4/14.....	Dog is quite sick, refuses to eat; perfusion stopped				

TABLE 7.—Data on Dog 2

Date	Cc. of 10% NaHCO <sub>3</sub>	First Specimen	Amylase Df		Control
			38 ° — 24 h		
4/11.....	...	...	.....	790	
4/14.....	150	530	1,712	...	
4/15.....	...	...	.....	380	
4/16.....	150	664	1,820	...	
4/18.....	150	260	1,960	...	
4/21.....	200	510	1,836	...	
4/22.....	...	...	.....	218	
4/23.....	300	370	2,108	...	
4/25.....	350	516	1,810	...	
4/28.....	400	226	2,322	...	
4/29.....	...	...	.....	280	
4/30.....	400	802	2,270	...	

In all cases, the first stool after the perfusion was soft and bulky and usually was passed within one hour. The second stool was passed from twelve to eighteen hours later and was normal in appearance. Fractions that amounted to less than five points were dropped from the results shown in the tables.

*Dogs 3 and 4.*—These animals were fed meals the same as dogs 1 and 2. From about eight to ten hours after the meal, the bowel was perfused with 1.25 per cent lactic acid. One attempt was made to perfuse during the ingestion of a meal, but 2.5 per cent lactic acid was used and after 150 cc. had been given, the dog vomited a large portion of the meal. Thereafter perfusions were given at night as already stated. The results are shown in tables 8 and 9.



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3. It is probable that the determination of fecal amylase will serve as a satisfactory method of determining pancreatic secretion when a specific stimulator that will produce complete uniform stimulation has been devised.

#### SUMMARY

1. The majority of the literature on pancreatic function tests has been reviewed, and some of the more important conclusions have been stated in this paper.

2. Determinations of fecal amylase were made on a series of normal persons to determine the normal value and its relation to the various factors concerned.

3. An attempt was made to establish a normal twenty-four hour fecal amylase value. The attempt was unsuccessful.

4. A series of cases was investigated and determinations of fecal amylase were made. Such conclusions as were evident have been stated in the foregoing work.

5. Animal experimentation was done to show that pancreatic stimulation can be demonstrated by determinations of fecal amylase.

#### CONCLUSIONS

1. Fecal amylase values of normal persons, using the Wohlgemuth-Hawk test, vary widely from day to day, depending largely on the diet.

2. In normal persons, the same diet produces closely similar stimulation to pancreatic secretion as shown by the values given on the same day by different persons on the same diet.

3. The weekly quantity of amylase secreted by normal persons on the same diet, as determined by determinations of fecal amylase, approaches a uniform value. That this is not a desirable procedure for clinical use, is evident.

4. The determinations of fecal amylase, Wohlgemuth-Hawk method, will show clinical results in only two types of cases: (a) cases of obstruction to the outflow of pancreatic juice; (b) cases in which a large portion of the gland is diseased so that it cannot supply sufficient amylase for normal digestive needs.

5. The determination of fecal amylase in dogs will show a quantitative increase in pancreatic secretion after gland stimulation by the application of lactic acid or sodium bicarbonate to the jejunum.

6. It is probable that a successful determination of fecal amylase can be devised, so that it will be of value in determining mild degrees of pancreatic involvement if the present work on secretin produces a purified, nontoxic product that can be used as a uniform stimulus for maximum pancreatic secretion; such maximum secretion to be determined by estimations of fecal amylase.

# THE CAUSE OF DEATH IN HIGH OBSTRUCTION\*

HENRY S. F. COOPER, M.D.

NEW YORK

What is the cause of death in high obstruction?

Why is it that a simple obstruction of the large intestine is compatible with life for a long time, while obstruction of the small intestine is rapidly fatal?

A tremendous amount of work has been done on this subject, which in turn has given rise to a multitude of theories, hardly two of which coincide. As in all problems for which a great number of explanations are offered, it is safe to assume that no one of them is entirely correct. Also, no theory has given rise to any practical means of preventing death after the condition has once fully established itself. In other words, no real advantage to the patient has accrued from this great mass of work. All medical and surgical research should have practical application as its ultimate goal. This goal is still in the dim distance as far as the work on high obstruction is concerned. Now, as always, prompt surgical intervention is the only means of combating this condition, and only too often this is of no avail.

The cause of death in high obstruction is not known. The object of this article is not to advance any one theory above the others; rather, is it an effort to present the subject in its many different phases and from its many different angles with the hope that somebody will see the spark and fan a flame that will bring light where there is darkness.

## CLINICAL AND PATHOLOGIC PICTURE

Patients suffering from uncomplicated obstruction of the small intestine rarely survive more than six or eight days if early surgical intervention does not take place. When the picture is fully developed, the following outstanding features present themselves:

The patient's psychology is often misleading. He is mentally alert and acutely aware of his surroundings. He does not realize the seriousness of his condition unless he is told. When first seen he is usually tossing about in bed. He is apt to talk about trivialities and make plans for the future. I have seen patients leave the hospital in this condition against the physician's advice.

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\* From the Department of Surgical Research, Cornell Medical School, New York.

\* This work was aided by a gift of Mrs. John L. Given in support of surgical research.

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There also are seasonal variations. For these reasons, it is not well to attach too much importance to minor differences in the length of survival. One animal that survives indefinitely is worth more as evidence than a hundred that survive a few days more than the normal span of life for the condition.

In order to have a working hypothesis it is first necessary to assume certain facts as established beyond a reasonable doubt. From a review of the literature on experimental work, it seems safe to concede the following facts:

FACTS OBTAINED FROM EXPERIMENTAL WORK IN THE  
LITERATURE

*Fact 1.*—Simple obstruction of the duodenum at a point just below the openings of the pancreatic and common bile ducts causes the most acute onset of symptoms and the earliest death. The length of survival and the acuteness of symptoms produced at other points in the small intestine is proportional to their proximity to this point.

Maury<sup>1</sup> was the first to demonstrate this fact. He established what he called the lethal line 35 cm. from the pylorus in dogs. Obstruction proximal or distal to this line he found to produce acute symptoms in proportion to its proximity. Incidentally, the line was below the openings of the pancreatic and common bile ducts. This was established on a series of over 400 animals.

Bunting and Jones<sup>2</sup> confirmed in substance these observations of Maury. Experimenting with rabbits, they found obstruction at the pylorus compatible with life for from thirty-six to forty-eight hours, while obstruction at points from the upper third of the duodenum to the middle of the jejunum caused death in from fifteen to twenty-four hours. Lesions at points below that gave progressively increasing lengths of survival.

Auché,<sup>3</sup> Dragstedt, Moorhead and Burcky,<sup>4</sup> Eisberg,<sup>5</sup> Sugito,<sup>6</sup>

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The patient usually looks acutely ill. His cheeks are sunken; his eyes are bright. In the later stages, he presents the typical hippocratic facies. There are beads of perspiration on his forehead. He often shows fibrillary twitchings of the hands and feet. His extremities are cold and clammy and his lips and nail-beds are often cyanotic. Usually, a deep coma intervenes before death.

Vomiting is a constant symptom. The vomitus first consists of gastric and duodenal contents and later takes on a fecal character, being light brown and of foul odor. At first the vomiting is accompanied by retching, but later it is passive, the material merely spilling from the patient's mouth. Persistent hiccups are often a distressing complication.

He may pass feces and gas in the early stages, but this soon gives way to persistent constipation.

The temperature is normal or subnormal; the pulse weak and rapid; respirations, shallow, and the blood pressure, low.

The red blood count is normal or increased, depending on the dehydration. There is leukopenia. The chemical examination of the blood gives a characteristic picture. The nonprotein nitrogen is high. This rise is almost entirely due to a marked rise in the urea. There may also be a rise in the creatinine. The chlorides are reduced. The carbon dioxide combining power is increased.

The urine is usually scanty, and often shows a trace of albumin or a few casts. The nonprotein nitrogen in the twenty-four hour specimen is much increased quantitatively, being often four or five times the normal amount. The chloride excretion is greatly reduced. The kidney function, as shown by the phenolsulphonphthalein test, is normal or slightly decreased.

The pathologic picture is curiously devoid of positive observations. The outstanding feature is marked splanchnic engorgement. The intestine, if not ruptured, is much dilated above the obstruction; its wall is dusky red and may present areas of gangrene. The lumen is full of sinking reddish-brown fluid which is rich in bacterial content. The mucosa is deeply injected and presents ulcerations. This condition is most marked immediately above the obstruction. Histologically, the intestinal wall shows marked capillary engorgement and areas of necrosis. Some observers have described fatty changes in the liver and evidences of toxic nephritis. These observations are not constant.

I shall next consider the experimental field. Before proceeding any further, it would be well to bring out the difficulties of animal experimentation. It is safe to assume that the condition can be reproduced in animals and that the picture is similar. Dogs lend themselves best to this type of experimentation. Cats and rabbits have been used, but the former are too resistant to the condition and the latter are too delicate. There is a great variation, however, in individual animals. Furthermore, animals in different localities seem to react differently.

**Stomach:** Dilated. Draper<sup>10</sup> and Hartwell and his co-workers<sup>11</sup> reported much capillary dilatation of the mucosa.

**Small Intestine:** There is marked splanchnic congestion. The portion above the obstruction is dusky red and much dilated. It contains large amounts of foul-smelling, red-brown fluid which is rich in bacteria. The mucosa is greatly injected all the way from the point of obstruction to the pylorus, presenting ulcerations and necrotic areas. Histologic examination shows round cell infiltration and hemorrhages (Hartwell and his co-workers<sup>11</sup>). The pathologic process is most marked just above the obstruction. The intestine below the obstruction is collapsed, but otherwise normal. Hartwell and his co-workers<sup>11</sup> also reported acute hyperplasia of the lymph follicles.

**Peritoneum:** Normal.

**Large Intestine:** Draper<sup>10</sup> described much capillary dilatation about the terminal colon. Nobody else reported this.

**Liver:** Hartwell and his co-workers<sup>11</sup> and Whipple and his co-workers<sup>7</sup> reported occasional congestion and fatty changes.

**Pancreas:** Hartwell and his co-workers<sup>11</sup> reported congestion. All other investigators reported the pancreas to be normal.

**Kidneys:** Brown, Eusterman, Hartman and Rowntree<sup>12</sup> reported evidence of severe toxic nephritis although they did not say what this evidence was. Hartwell and his co-workers<sup>11</sup> reported marked congestion and the presence of granular coagula in the tubules. South and Hardt<sup>13</sup> reported cloudy swelling. Draper<sup>10</sup> and Whipple and his co-workers<sup>7</sup> reported normal kidneys.

**Spleen:** South and Hardt<sup>13</sup> reported the spleen to be swollen. All others reported it to be normal.

There is not by any means a unanimity of opinion on this subject, but nevertheless, it was felt best to include the pathologic description under the facts.

**Fact 5.**—If a segment of small intestine is isolated and the ends inverted, and if then the continuity of the intestinal tract is reestablished by anastomosis, the animal will present a picture in a general way similar to an obstruction at the level from which the segment was isolated.

This fact was first brought out clearly by Whipple and his co-workers<sup>7</sup> and has been confirmed by many investigators since, most

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10. Draper, J. W.: Studies in Intestinal Obstruction with a Report of Feeding Heterologous Jejunal and Ileac Cells to a Human Being, *J. A. M. A.* 63:1079 (Sept. 26) 1914.

11. Hartwell, J. A.; Hoguet, J. P., and Beckman, F.: An Experimental Study of Intestinal Obstruction, *Arch. Int. Med.* 13:701 (May) 1914.

12. Brown, G. E.; Eusterman, G. B.; Hartman, H. R., and Rowntree, L. G.: Toxic Nephritis in Pyloric and Duodenal Obstruction, *Arch. Int. Med.* 32:425 (Sept.) 1923.

13. South, E. L., and Hardt, L. L. J.: Experimental Intestinal Obstruction, *Arch. Int. Med.* 21:292 (Feb.) 1918.

Whipple and his co-workers<sup>7</sup> and many others have agreed in general with this, but have been content with stating that the higher the obstruction the more rapidly fatal the outcome.

*Fact 2.*—Experimental animals suffering from high obstruction show the following clinical picture:

- (1) They vomit.
- (2) They become dehydrated.
- (3) They show tremors and weakness of the hind legs.
- (4) The pulse becomes weak and rapid.
- (5) The blood pressure falls.
- (6) The urine is scanty.
- (7) Coma precedes death.

All these symptoms have been so frequently observed that it does not seem necessary to quote references.

*Fact 3.*—A study of the clinical pathology of animals suffering from obstruction shows the following picture:

**Blood:**

- (1) Leukopenia.
- (2) Slightly increased fibrin.<sup>8</sup>
- (3) High nonprotein nitrogen, almost entirely due to an increase in urea.
- (4) Low chloride content.
- (5) High carbon dioxide combining power.

**Urine:**

- (1) Scanty.
- (2) Slight trace of albumin.
- (3) Nonprotein nitrogen excretion much increased.
- (4) Low chloride excretion.
- (5) Trace of phenol and indican.

With the exception of item 2 in the description of the blood, all the items are based on the observations of many workers.

*Fact 4.*—An animal that has died of high obstruction shows the following pathologic picture:

Central Nervous System: Normal, grossly and microscopically.

Lungs: Normal, grossly and microscopically.

Heart: Normal, grossly and microscopically.

Blood Vessels: Williams reported<sup>9</sup> hemolytic staining of the intima of the arteries.

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7. Stone, H. B.; Bernheim, B. M., and Whipple, G. K.: Intestinal Obstruction: A Study of the Toxic Factors. *Bull. Johns Hopkins Hosp.* **23**:159, 1912.

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9. Williams, B. W.: Importance of Toxemia Due to Anaerobic Organisms in Intestinal Obstruction and Peritonitis. *Brit. J. Surg.* **14**:205, 1926-1927.



Whipple and his co-workers<sup>24</sup> did many experiments in which they demonstrated a rise in the urea. Gatch, Trusler and Ayers<sup>25</sup> reported a slight fall in the chlorides. Nobody else reported any change in the chlorides or in carbon dioxide combining power.

*Fact 6.*—If there is an interference in the circulation at the point of obstruction (i.e., strangulation), the picture is much more acute and death much more rapid.

The great difference between strangulation and simple obstruction has been recognized by many workers (Brooks and co-workers,<sup>20</sup> Foster and Hausler,<sup>26</sup> Hartwell and his co-workers,<sup>27</sup> Howell,<sup>28</sup> Murphy and Vincent,<sup>29</sup> Reichel,<sup>30</sup> Sugito<sup>6</sup> and Wilkie<sup>31</sup>).

Whether or not high strangulation is more fatal than low is not so clearly demonstrated; however, it probably is. This is difficult to demonstrate because the symptom complex is so acute that the picture is telescoped in as far as time is concerned, and therefore variations in the length of survival are correspondingly more difficult to demonstrate. However, a few references to it are found in the literature (Scholefield,<sup>32</sup> Schönbauer<sup>33</sup>).

There are further variations in the clinical aspect that are similar to, but more marked than, those described under fact 5.

1. The shorter the strangulated segment, the more rapid is the onset of symptoms and the more fatal the outcome (Brooks and his co-workers,<sup>20</sup> Scholefield,<sup>32</sup> Sugito<sup>6</sup>).

24. Cooke, J. V.; Rodenbaugh, F. H., and Whipple, G. H.: Intestinal Obstruction: VI. A Study of Noncoagulable Nitrogen of the Blood, *J. Exper. Med.* **23**:717, 1916.

25. Gatch, W. D.; Trusler, H. M., and Ayers, K. D.: Acute Intestinal Obstruction: Mechanism and Significance of Hypochloremia and Other Blood Chemical Changes, *Am. J. M. Sc.* **73**:649, 1927.

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27. Hartwell, J. A.: Intestinal Obstruction, *J. Exper. Med.* **18**:139, 1913. Hartwell and Hoguet (footnote 17).

28. Howell, J.: Experimental Observations on the Cause of Death in Acute Intestinal Obstruction, *Brit. M. J.* **2**:1645, 1913.

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30. Reichel, P.: Zur Pathologie des Ileus und Pseudoileus, *Deutsche Ztschr. f. Chir.* **35**:495, 1892-1893.

31. Wilkie, D. P. D.: Experimental Observations on the Cause of Death in High Obstruction, *Brit. M. J.* **2**:1064, 1913.

32. Scholefield, B. G.: Acute Intestinal Obstruction: Experimental Evidence of the Absorption of Toxin from Obstructed Bowel, with a Critical Review of Various Methods of Treatment, *Guy's Hosp. Rep.* **77**:160, 1927.

33. Schönbauer, L.: Die Fermente in ihrer Beziehung zu gewissen Erkrankungen der Gallenblase und zum Ileus, *Arch. f. klin. Chir.* **130**:427, 1924.

prominently by Bunting and Jones,<sup>14</sup> Dragstedt, Dragstedt and co-workers,<sup>15</sup> Eisberg,<sup>5</sup> and Murphy and Brooks.<sup>16</sup>

The statement was made that the picture, in a general way, was similar to that in obstruction. The following variations occur:

1. Colonic and low ileal closed loops are compatible with life indefinitely (Halsted, von Baracz, quoted from Hartwell and his co-workers,<sup>17</sup> Murphy and Brooks,<sup>16</sup> Whipple<sup>18</sup> and Wilkie<sup>19</sup>).

2. The length of the closed loop brings in another factor. Animals with short loops die sooner than those with long ones (Brooks and his co-workers,<sup>20</sup> Dragstedt, Dragstedt and co-workers<sup>21</sup>).

3. Sometimes an animal will survive indefinitely with a closed loop no matter where it is (Dragstedt, Dragstedt and co-workers,<sup>4</sup> Sweet<sup>22</sup>). It seems as if this would have to be laid to individual variation. An animal has never survived when the closed loop received the secretion of the liver and pancreas.

4. Animals with closed loops show a slightly different picture from animals with simple obstruction. They do not vomit as much, they do not become as dehydrated (Ingvaldsen and co-workers<sup>6</sup> and others), and the changes in the blood and urine chemistry are not as marked. Copher and Brooks<sup>23</sup> reported cases of dogs dying without changes.

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14. Bunting, C. H., and Jones, A. P. (footnote 2, second reference).

15. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: *Intestinal Obstruction: II. A Study of the Factors Involved in Production and Absorption of Toxic Materials from the Intestine*, *J. Exper. Med.* **30**:109, 1919 (footnote 4).

16. Murphy, F. T., and Brooks, B.: *Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death*, *Arch. Int. Med.* **15**:392 (March) 1915.

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20. Brooks, B.; Schumacher, H. W., and Wattenberg, J. E.: *Intestinal Obstruction: An Experimental Study*, *Ann. Surg.* **67**:210, 1918.

21. McClintock, J. T.; Dragstedt, L. R., and Dragstedt, C. A.: *Some Results from the Experimental Study of Intestinal Obstruction*, *J. Iowa State M. Soc.* **9**:8, 1919.

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23. Copher, G. H., and Brooks, B.: *Intestinal Obstruction: An Experimental Study of the Therapeutic Value of the Administration of Sodium Chloride*, *Ann. Surg.* **78**:755, 1923.

Stone,<sup>37</sup> Whipple and his co-workers<sup>7</sup> and others. These facts are well established.

*Fact 8.*—The intestinal content of an animal that has died of toxic injection is also toxic when prepared and injected in a similar way. The clinical and pathologic picture is identical with that described under fact 7. This process can be repeated indefinitely, the toxin always being recoverable from the intestinal content of an animal that has died from its injection.

This fact has been established by Ellis<sup>38</sup> and by Sweet<sup>39</sup> on the basis of many experiments. Other workers have not studied it, but there are no conflicting opinions.

*Fact 9.*—The content of normal dogs during fasting is only slightly toxic when prepared in the same way.

There is some dissension on this point. Opinions vary all the way from claims that the normal content is absolutely innocuous to statements that it is more toxic than obstruction content.

Clairmont and Ranzi,<sup>39</sup> Davis and Stone,<sup>40</sup> Dragstedt, Dragstedt and co-workers,<sup>41</sup> Ellis,<sup>38</sup> Sugito<sup>6</sup> and Whipple and his co-workers<sup>42</sup> claimed that normal content is absolutely nontoxic if prepared and injected while it is still fresh.

Cybulski and Tarchanoff,<sup>43</sup> Davis,<sup>44</sup> Falloise<sup>45</sup> and Kukula<sup>46</sup> claimed that there is a slight but definite toxicity to the normal content.

37. Stone, H. B.: The Toxic Agents Developed in the Course of Acute Intestinal Obstruction and Their Action, *Surg. Gynec. Obst.* 32:415, 1921.

38. Sweet, J. E.: Intestinal Obstruction, Experimental Research, *Internat. Clin.* 1:72 (30th ser.) 1920.

39. Clairmont, P., and Ranzi, E.: Zur Frage der Autointoxication bei Ileus. *Arch. f. klin. Chir.* 73:696, 1904.

40. Davis, D. M., and Stone, H. B.: Studies on the Development of Toxicity in Intestinal Secretion, *J. Exper. Med.* 26:687, 1917.

41. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Extirpation of the Duodenum, *Am. J. Physiol.* 46:584, 1918. Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: The Nature of the Toxemia of Intestinal Obstruction: Preliminary Report, *Proc. Soc. Exper. Biol. & Med.* 14:17, 1916-1917.

42. Whipple, G. H.; Stone, H. B., and Bernheim, B. M.: Intestinal Obstruction, *J. Exper. Med.* 17:307, 1913.

43. Cybulski, N., and Tarchanoff, J.: A propos des poisons normaux de l'intestin. *Arch. internat. de phys.* 5:257, 1907.

44. Davis, D. M.: Intestinal Obstruction: Formation and Absorption of Toxin. *Bull. Johns Hopkins Hosp.* 25:33, 1914.

45. Falloise, A.: Les poisons normaux de l'intestin chez l'homme et les moyens de defense contre ces poisons, *Arch. Internat. de physiol.* 5:159, 1907.

46. Kukula, O.: Untersuchungen über Autointoxicationen bei Darmocclusionen. *Arch. f. klin. Chir.* 63:773, 1901.

2. Animals with strangulation show the following variations from the picture in simple obstruction: They do not become dehydrated, and the changes in the chemistry of the blood and urine are less marked. There is, however, usually a rise in the urea (Whipple and his co-workers,<sup>24</sup> Foster and Hausler,<sup>25</sup> Gatch, Trusler and Ayers<sup>25</sup>). Copher and Brooks<sup>16</sup> reported death in strangulation without blood changes. Nobody reported any changes in the blood chlorides or carbon dioxide.

**Fact 7.**—The intestinal content from above the obstruction, or from a closed loop or from a strangulated loop, after being prepared in one of any number of ways and injected into another animal (preferably intravenously) will cause the rapid death of that animal with a typical clinical and pathologic complex which is as follows:

**Clinical:**

- (1) Vomiting.
- (2) Tenesmus and bloody diarrhea.
- (3) Dilatation of the pupils.
- (4) Tremor, weakness of the hind legs.
- (5) Pulse, weak and rapid.
- (6) Death.

**Blood:**

- (1) Coagulation reduced.
- (2) Rapid rise of nonprotein nitrogen, mostly due to urea.

**Urine:**

- (1) Increase in amount.<sup>24</sup>
- (2) Slight trace of albumin.<sup>24</sup>
- (3) Sharp rise in nonprotein nitrogen excretion.<sup>24</sup>

**Pathologic Observations:**

- (1) Blood concentrated and clots slowly.
- (2) Spleen, liver and pancreas engorged; liver may be tense and friable.
- (3) Splanchnic vessels very prominent.
- (4) Stomach may be injected about the cardia.
- (5) The greater part of the mucosa of the small intestine presents a red, velvety appearance. This starts at a definite line 1 cm. below the pylorus, is most marked in the duodenum and gradually fades out toward the terminal ileum.
- (6) There is an effusion of blood-stained fluid into the lumen of the small intestine.

Albeck<sup>22</sup> was the first to describe the toxic qualities of this material. This has been almost universally observed since. The clinical and pathologic pictures are fully described by Ellis,<sup>26</sup> Murphy and Vincent,<sup>27</sup>

<sup>24</sup> Whipple and Coker: Protozo Intoxication and Injury to Body Proteins I—Metabolism of Fasting Dogs After Protozo Injections, *J. Exper. Med.* **25**:461, 1917.

<sup>25</sup> Albeck, V.: Experimentelle und klinische Untersuchungen über die Toxikologie bei Duodenalstrangulation, *Arch. f. klin. Chir.* **45**:560, 1902.

<sup>26</sup> Ellis, J. W.: Cause of Death in High Intestinal Obstruction, *Ann. Surg.* **75**:429, 1922.

over long periods of time. At subsequent postmortem examination, they were able to isolate the same organisms from the viscera. They thus concluded that bacteria could enter the blood from the intestinal lumen. Borszesky and Genersich<sup>50</sup> claimed to recover colon bacilli from the blood in a large percentage of subjects dying from high obstruction. They therefore concluded that this was the cause of death. Later investigation has shown that this is apt to be a terminal event in any death. Also, many workers since have definitely proved, by repeated sterile cultures that such a bacterial invasion does not exist in acute intestinal obstruction. The most conclusive of this evidence is seen in the work of Hartwell, Hoguet and Beckman.<sup>11</sup>

A study of these facts immediately stimulates thought and gives rise to many questions that need answering. The answers, unfortunately, are not easily forthcoming. Most of them are still being sought.

#### QUESTIONS CONCERNING CAUSE OF DEATH IN HIGH OBSTRUCTION

*Question 1.*—Why is it that the higher the obstruction the more rapidly death occurs?

This is the most fundamental and far-reaching question. If it could be answered, the cause of death in high obstruction would be known. I shall not attempt to discuss it here, but will let the reader attempt to find an answer in the theories that are to be developed later.

*Question 2.*—What is the explanation of the clinical picture?

Vomiting may be explained by the presence of the obstruction. The intestinal content comes up because it cannot go down. Peristalsis forces the material against the barrier, and a return flow results in the center of the stream. The vomitus is really squeezed out through the only available exit, which is the mouth. There may also be a toxic factor in this vomiting which will be taken up in detail later.

Dehydration is the direct result of the vomiting. Hartwell<sup>11</sup> showed this clearly. Braun and Boruttau<sup>40</sup> emphasized the fact that the secretion produced by the normal intestine in twenty-four hours is equivalent to almost the entire amount of blood and lymph in the body. The reabsorption of this fluid is the only reason that the normal body is not continually and progressively dehydrated. If, then, this reabsorption is prevented by obstruction, it is easy to see why an extreme dehydration results.

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56. Borszesky, C., and von Genersich, A.: Beiträge zur Lokaldiagnose der inneren Darmokklusionen und zur Frage der Autointoxikation, Beitr. z. klin. Chir. 36:448, 1902.

Roger and Garnier;<sup>47</sup> Wangensteen and Chunn<sup>48</sup> asserted that the normal content is at least as toxic as contents after obstruction.

Braun and Boruttau<sup>49</sup> maintained that the normal content is more toxic than obstruction content.

In view of these statements gleaned from the literature, it was thought best to strike a mean and say that the normal content may be toxic.

*Fact 10.*—Large amounts of this toxin may be introduced into the lumen of the normal small intestine without untoward results.

This fact is universally accepted without dissension. It has been amply proved by Davis,<sup>44</sup> Schönbauer,<sup>33</sup> Stone,<sup>27</sup> Whipple and his co-workers,<sup>50</sup> and Wilkie.<sup>51</sup>

*Fact 11.*—Death in high obstruction, closed loops and strangulation can occur without bacterial infection of the peritoneum or blood stream.

That death was due to peritonitis was held to be the case by some of the earlier observers. Albarran and Caussade<sup>52</sup> felt that this was true. They claimed that if bacteria did not get through gross openings in the wall of the intestine they found their way through the intact structure with a resulting peritonitis. This has been emphatically and completely disproved. Buchbinder<sup>53</sup> and Helmberger and Martina<sup>54</sup> were among the first to disprove this contention. The permeability of the intestinal wall to bacteria will be discussed more fully.

Some of the early workers believed also that septicemia played a part in the picture. Wrzosek<sup>55</sup> fed nonvirulent organisms to dogs

47. Roger, H., and Garnier, M.: Les poisons du tube digestif, *Rev. de méd.* 26:953, 1906.

48. Wangensteen, O. H., and Chunn, S. S.: Studies in Intestinal Obstruction: I. A Comparison of the Toxicity of Normal and Obstructed Intestinal Content, *Arch. Surg.* 16:606 (Feb.) 1928.

49. Braun, W., and Boruttau, H.: Experimentell-kritische Untersuchungen über den Ileustod, *Deutsche Ztschr. f. Chir.* 96:544, 1908.

50. Whipple, G. H.: Intoxication of Intestinal Obstruction, *Contrib. Med. & Biol. Research*, Sir W. Osler, New York 2:1065, 1919. Whipple: Stone and Bernheim (footnote 42).

51. Wilkie (footnotes 31 and 19).

52. Albarran, J., and Caussade, G.: Étude expérimentale sur les obstructions intestinales aiguës, xiii Cong. int. de méd., *Compt. rend., Paris* (Sect. de path. gén. et expér.) 2:583, 1900.

53. Buchbinder, H.: Experimentelle Untersuchungen am lebenden Thier- und Menschendarm, *Deutsche Ztschr. f. klin. Chir.* 55:458, 1900.

54. Helmberger, A., and Martina, A.: Experimentelle Untersuchungen über die Durchlässigkeit des Darmes für Bakterien, *Deutsche Ztschr. f. Chir.* 74:527, 1904.

55. Wrzosek, Adam: Experimentelle Beiträge zur Lehre von dem latenten Mikrobismus, *Virchows Arch. f. path. Anat.* 175:82, 1904.

amounts to a 1,000 per cent increase, whereas the concentration of the blood as measured by hematocrit readings does not indicate a change even worth considering in this comparison (White and Bridge<sup>61</sup>).

One is forced to the conclusion that urea is being formed to a great excess somewhere in the body. Urea is formed from the breaking up of amino-acids, which in turn come from a splitting of the protein molecule. From this one must further deduce that the high urea content in this case is an index of a rapid destruction of protein or amino-acids, so rapid in fact, that the kidney excretion cannot keep up with it even though it be working overtime.

Analogous conditions (i. e., high blood urea accompanied by high nitrogen excretion) are described as follows:

- (1) Injection of toxins obtained from the lumen of the gut above an obstruction (Whipple and Cooke<sup>62</sup>).
- (2) Simple laparotomy (Whipple, Cooke and Stearns<sup>63</sup>).
- (3) Sterile abscess (Cooke and Whipple<sup>64</sup>).
- (4) Pleuritis (Cooke and Whipple<sup>64</sup>).
- (5) Pancreatitis (Cooke and Whipple<sup>64</sup>).
- (6) Bilateral suprarenalectomy (Stewart and Rogoff<sup>65</sup>).
- (7) Anaphylaxis (Weil<sup>66</sup>).

Also, a high blood urea without kidney impairment is described by Cooke and Whipple<sup>64</sup> in pneumonia and acute yellow atrophy.

Another interesting point which will be discussed more fully is the fact that if a dog suffering from high simple obstruction is given fluids, especially saline infusion, the urea immediately shows a marked decrease and may even reach normal even though the obstruction still exists. This will be discussed more fully later.

#### *Question 6.—Why does all this destruction occur?*

Whipple and his co-workers expressed the opinion that it is the result of the action of some toxic body on the tissues. They explained that this may be a rather nonspecific reaction since it is seen in so many different conditions. They offered an explanation of the fact that the administration of the fluid lowers the urea by asserting that it causes a dilution of the toxins with a resultant diminution of their

61. White, J. C., and Bridge, E. M.: Loss of Chloride and Water from the Tissues and Blood in Acute High Intestinal Obstruction, *Boston M. & S. J.* 196: 893, 1927.

62. Cooke, J. V., and Whipple, G. H.: Proteose Intoxication: IV. Metabolism of Dogs with Sterile Abscess, Pancreatitis and Pleuritis, *J. Exper. Med.* 28: 223, 1918.

63. Stewart, G. N., and Rogoff, J. M.: Studies on Adrenal Insufficiency, *Proc. Soc. Exper. Biol. & Med.* 22:394, 1924.

64. Weil, R.: Studies in Anaphylaxis: XXI. Anaphylaxis in Dogs; A Study of the Liver in Shock and in Peptone Poisoning, *J. Immunol.* 2:525, 1917.

The tremors and weakness, the weak rapid pulse, the low blood pressure and the coma will be taken up in detail later. It does not seem as if they could be explained entirely on the grounds of dehydration.

*Question 3.*—Why does leukopenia occur?

No explanations have been offered for this phenomenon. It is, however, evidence against the probability of an infective process being the cause of death.

*Question 4.*—Why is the fibrin increased?

No explanation of this fact is forthcoming.

*Question 5.*—Why does high blood urea occur?

This phenomenon of high obstruction was first described by Tileston and Comfort<sup>57</sup> in 1914. Cooke, Rodenbaugh and Whipple<sup>24</sup> were the next to call attention to it. The latter workers also concluded that this rise was proportional to the seriousness of the symptoms.

Of course, whenever the blood urea increases, one immediately thinks of impaired kidney function. In this case it would have to be considerably impaired to cause the degree of apparent retention that is so often seen. The answer is that retention of urea does not occur, but rather a greatly increased formation. Haden and Orr<sup>58</sup> and Whipple, Cooke and Stearns<sup>59</sup> have conclusively demonstrated that the nitrogen excretion of the urine in cases of obstruction as measured in the twenty-four hour specimen is four or five times the normal amount. That there may be slight kidney damage was demonstrated by McQuarrie, Irvine and Whipple.<sup>60</sup> After careful investigation, they determined that the kidney function as measured by its ability to excrete phthalein, urea and sodium chloride was slightly but definitely decreased. The presence of albuminuria, an occasional cast and a slightly increased amount of creatinine may be taken as further evidence of slight damage. However, all those who claim that there is serious renal damage have to explain how such a compromised kidney can excrete four or five times the normal amount of urea.

The next most obvious explanation is dehydration and the resulting concentration of the blood. In the first place, the rise in urea often

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57. Tileston, W., and Comfort, C. W. Jr.: The Total Nonprotein Nitrogen of Urea of the Blood in Health and Disease as Estimated by Folin's Methods, *Arch. Int. Med.* 14:620 (Nov.) 1914.

58. Haden, R. L., and Orr, T. G.: The Cause of Certain Acute Symptoms Following Gastro-Enterostomy, *Bull. Johns Hopkins Hosp.* 34:26, 1923.

59. Whipple, G. H.; Cooke, J. V., and Stearns, T.: Proteose Intoxication and Injury of Body Protein: II. Metabolism of Dogs with Duodenal Obstruction and Isolated Loops, *J. Exper. Med.* 25:479, 1917.

60. McQuarrie, I., and Whipple, G. H.: I. Renal Function Influenced by Intestinal Obstruction, *J. Exper. Med.* 29:397, 1919. ✓



Haden and Orr<sup>70</sup> demonstrated that reduction of chlorides was a constant observation in all cases of simple high obstruction. They further brought out the following facts:

(1) Lowering of chlorides is the first change in the blood chemistry following simple high obstruction, coming before the rise in urea.

(2) The higher the obstruction, the more rapid the loss of chlorides.

(3) They were able to keep dogs with duodenal obstruction alive from twenty-one to twenty-eight days with the subcutaneous administration of 500 cc. of 0.9 per cent salt solution a day. (Death at the end of this period might easily be attributed to starvation.)

(4) As long as they kept the blood chlorides at a normal level by the administration of saline, the other blood changes did not occur.

(5) Dogs in which an attempt to make up the loss of fluid was made by the administration of solutions of dextrose or sodium bicarbonate, died more quickly than animals which were untreated.

(6) Animals did not derive any benefit from attempts to repair the loss of fluid by the administrations of potassium chloride, ammonium chloride, calcium chloride or magnesium chloride.

(7) Animals with obstruction in which no attempt was made to make up the loss of fluid, but in which the loss of chloride was made up by small amounts of concentrated sodium chloride solution (50 cc. 10 per cent sodium chloride per diem), lived from twenty-one to twenty-eight days and did not show toxemia or blood changes.

They applied this form of treatment to patients suffering from high obstruction and found that it probably prolonged life in some cases. In its clinical application, they advised the administration of 1 Gm. of

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70. Haden and Orr (footnote 58); Chemical Changes in the Blood of the Dog After Intestinal Obstruction, *J. Exper. Med.* 37:365, 1923; Chemical Changes in the Blood of the Dog After Pyloric Obstruction, *ibid.* 37:377, 1923; The Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, *ibid.* 38:55, 1923; Chemical Changes in the Blood of the Dog After Obstruction of the Esophagus and the Cardiac End of the Stomach, *ibid.* 38:477, 1923; Chemical Changes in the Blood of Man After Acute Intestinal Obstruction, *Surg. Gynec. Obst.* 37:465, 1923; The Effect of Inorganic Salts on the Chemical Changes in the Blood of the Dog After Obstruction of the Duodenum, *J. Exper. Med.* 39:321, 1924; Use of Sodium Chloride in Treatment of Intestinal Obstruction, *J. A. M. A.* 82:1515 (May 10) 1924; Obstruction of the Jejunum: Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog, *Arch. Surg.* 11:859 (Dec.) 1925; Experimental High Intestinal Obstruction in the Monkey, *J. Exper. Med.* 41:107, 1925; Distribution of Chlorides in the Blood of the Dog After Experimental Intestinal Obstruction, *ibid.* 41:113, 1925; The Sodium Content of the Blood of the Dog After Experimental Intestinal Obstruction, *ibid.* 41:119, 1925; Experimental Obstruction of the Jejunum: Effect of Sodium Chloride Injected into Lumen of Intestines Below Obstruction, *ibid.* 41:707, 1925; Effect of Jejunostomy on Experimental Obstruction of the Jejunum of the Dog, *ibid.* 43:483, 1926; Blood Fibrin in Upper Gastro-Intestinal Tract Obstruction, *ibid.* 45:427, 1927; Excretion of Nitrogen After Upper Gastro-Intestinal Obstruction, *ibid.* 45:433, 1927; Treatment of Toxemia of Intestinal Obstruction, *Colorado Med.* 21:140, 1924.

activity. This theory, in substance, is concurred in by Haden and Orr,<sup>65</sup> McVicar<sup>66</sup> and Rabinowitch.<sup>66</sup>

Gamble and Ross<sup>67</sup> expressed the opinion that the high urea was the result of dehydration and impaired renal function. Brown, Eusterman, Hartman and Rowntree<sup>12</sup> thought that kidney impairment is the overwhelming factor. None of these workers, however, gives any reports on the excretion of urinary nitrogen, nor do they give details of the pathologic process discovered in the kidneys. This would seem important.

Hartmann and Sniyth<sup>67a</sup> approached the problem from a slightly different angle. They suggested that the urea appears in the blood to compensate, in some rather obscure manner, for the loss of chloride. They inferred that it may have some action either in the acid-base mechanism or in keeping the osmotic relations in proper balance.

Bacon, Anslow and Eppler<sup>68</sup> mentioned the fact that there are rises in the urea in any condition calculated to cause dehydration. They killed dogs in a few hours by hypertonic saline infusion and the resultant dehydration. They noticed a rise in urea in these cases and attributed it to loss of water. They offered the following explanation: In dehydration, the water of hydration is removed from the protein molecule to make up for the deficiency. This may result in the disintegration of the protein molecule with an accompanying formation of urea. This theory sounds very well, but its application as a possible explanation of the high amount of urea in obstruction is weakened by the fact that they noticed a marked hyperpyrexia in all their cases. This, of course, does not occur in obstruction.

*Question 7.*—Why do the blood chlorides decrease?

MacCallum, Lintz, Vermilye, Leggett and Boas<sup>69</sup> first demonstrated low amounts of chlorides in their work on pyloric obstruction. From their researches they also showed a definite benefit derived from the administration of chloride.

65. McVicar, C. S.: A Discussion of the Clinical and Laboratory Clinical Findings in Certain Cases of Obstruction in the Gastro-Intestinal Tract: The Rôle of Blood Chemistry in Diagnosis, Prognosis and Treatment of this Condition, *Am. J. M. Sc.* **169**:224, 1925.

66. Rabinowitch, I. M.: The Prognostic Value of the Study of the Blood Chemistry in the Acute Abdomen, *Canad. M. Ass. J.* **11**:163, 1921.

67. Gamble, J. L., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, *J. Clin. Invest.* **1**:403, 1925.

67a. Hartmann, A. F., and Smyth, F. S.: Chemical Changes in the Body Occurring as the Result of Vomiting, *Am. J. Dis. Child.* **32**:1 (July) 1926.

68. Bacon, D. K.; Anslow, R. E., and Eppler, H. H.: Intestinal Obstruction, *Arch. Surg.* **3**:641 (Nov.) 1921.

69. MacCallum, W. G.; Lintz, J.; Vermilye, H. N.; Leggett, T. H., and Boas, E.: The Effect of Pyloric Obstruction in Relation to Gastric Tetany, *Bull. Johns Hopkins Hosp.* **31**:1, 1920.

discovered and failed to bring out, and the other of which they overlooked. In the first place, they showed that the administration of chlorides in forms other than sodium chloride did no good. In the second place, animals dying from high obstruction without vomiting have greatly dilated stomachs and upper intestines which are filled with large amounts of fluid.

However, in favor of their theory of a detoxifying action of chloride are the following observations:

Peabody<sup>74</sup> observed a fixation of the chlorides in the tissues in pneumonia.

Loeb (quoted from Hastings, Murray and Murray<sup>75</sup>) discovered that the toxicity for the adult *Fundulus* of sodium bromide, sodium sulphate and sodium nitrite was abolished by adding sodium chloride.

Sugito<sup>6</sup> reported that the toxicity of intestinal contents after obstruction was lost when the substance was dialyzed for several hours through a collodion sac against physiologic sodium chloride solution. He further reported that the toxin formed crystals with the chlorides of heavy metals.

Another interesting side-light is seen in the fact that Rackemann, Longcope and Peters<sup>76</sup> found low amounts of chlorides in serum sickness.

On the other hand, Copher and Brooks<sup>23</sup> and Gatch, Trusler and Ayers<sup>25</sup> and others pointed out that the administration of the chloride does not do any good in the treatment of strangulation. Furthermore, Copher and Brooks<sup>23</sup> did not find any loss of chlorides in animals dying from toxic injection. In addition, they mixed the toxic substance with sodium chloride and injected it without any diminution in its effect. They also could not demonstrate any beneficial effect if large amounts of sodium chloride were administered subcutaneously and intraperitoneally before and after toxic injection.

Gatch, Trusler and Ayers<sup>25</sup> made careful quantitative examination of the vomitus, urine, blood and tissues in cases of obstruction. They found that the tissue chlorides were reduced in the same proportion as the blood chlorides. They further found that there was enough loss of chloride in the urine and vomitus to account easily for this reduction. They observed the same thing to be true of the chloride content

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74. Peabody, F.: Studies of the Inorganic Metabolism in Pneumonia With Especial Reference to Calcium and Magnesium, *J. Exper. Med.* 17:71, 1913.

75. Hastings, H. B.; Murray, C. D., and Murray, H. A.: Certain Chemical Changes in the Blood After Pyloric Obstruction in Dogs, *J. Biol. Chem.* 46:223, 1921.

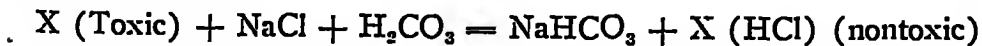
76. Rackemann, F. M.; Longcope, W. T., and Peters, J. P.: The Excretions of Chlorides and Water and the Renal Function in Serum Disease, *Arch. Int. Med.* 18:496 (Oct.) 1916.

sodium chloride per kilogram of body weight by infusion or hypodermoclysis of a 3 per cent solution as an initial dose. After that it should be administered as the occasion arises to keep the blood chlorides at a normal level. This stands as a definite clinical aid in the treatment of subjects with simple obstruction.

Foster and Hausler<sup>71</sup> brought up an interesting variation. They felt that the loss of chloride was apt to occur only in what they called the "critical period." This, they stated, corresponded to the healing period of intestinal wounds in experimental animals and lasted for four or five days after operation. In their experiments, they took great care to keep the blood chlorides at the proper level for the first five days after operation. Animals treated in this way survived for periods of three or four weeks even when chlorides or water were not administered after the critical period. This work was corroborated by Gatch, Trusler and Ayers.<sup>22</sup>

Hartwell and Hoguet<sup>72</sup> stumbled on the value of chloride therapy ten years before Haden and Orr started their investigations. They reported that they could keep dogs with high obstruction alive for three or four weeks by making up for the loss of fluid. In order to do this, they gave large amounts of physiologic sodium chloride solution. It did not occur to them that the sodium chloride was an important factor.

Haden and Orr<sup>73</sup> then tried to account for this loss of chlorides. They did quantitative tests on the urine and vomitus and decided that enough was not lost by these avenues. They then observed that loss of chloride and toxemia resulted in obstructed monkeys and rabbits.<sup>73</sup> Rabbits cannot vomit. Monkeys were not observed to vomit. Building their theory on this basis, they decided that the Cl ion ( $\text{Cl}^-$ ) acted as a specific antibody on some toxin that was circulating in the blood as a result of the obstruction. They conceived of the reaction as being somewhat like this:



Thus, they believed, a large amount of chloride is held in the tissues. This toxin, they thought, caused a destruction of protein with the formation of urea. When the toxin was neutralized by administration of the chloride, the excess urea was excreted and no more was formed. There are two weaknesses in this theory, one of which they themselves

71. Foster, W. C., and Hausler, R. W.: Acute Intestinal Obstruction: III. Simple Obstruction, *Arch. Int. Med.* **36**:31 (July) 1925.

72. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution, *J. A. M. A.* **59**:82 (July 13) 1912.

73. Haden and Orr (footnote 70, tenth reference).

Portis and Portis<sup>78</sup> described an elaborate experiment whereby they produced an isolated loop of duodenum which they were able to wash out and drain at will. They demonstrated a marked loss of hydrochloric acid from the loop with the early development of the symptoms of tetany and death. They found that they could prevent this sequel, or stop it if it had already begun, by introducing 0.3 per cent hydrochloric acid into the loop in appropriate quantities. They forget, however, that a dog with a drained duodenal loop is apt to live indefinitely anyway.

Gamble and his co-workers<sup>79</sup> went a step farther. They studied the base-forming elements of the body which tend to offset the acid forming elements in maintaining the acidity of the blood at the proper equilibrium. They found them to be as follows in the approximate proportions indicated:  $\text{Na}^+$ , 90 per cent;  $\text{Ca}^{++}$ , 4 per cent;  $\text{K}^+$ , 3 per cent;  $\text{Mg}^{++}$ , 3 per cent. They emphasized the fact that there is no easy means of altering the base concentration as there is on the acid side. It is all relatively fixed. They concluded, therefore, that when base is lost, water must be lost at the same time in order to keep the base concentration at the proper level and maintain the acidity which is essential for life. They then investigated the various avenues by which base might be lost. They killed rabbits by producing high obstruction and examined the contents of their stomachs. Here they found a fluid which contained base, mostly in the form of sodium, chloride and water which represented losses equal to several times the initial total plasma content of each of these elements.

It seems, therefore, that the high carbon dioxide combining power is due to a loss of chloride and that the dehydration is due to a loss of water. Also, the fact that only water and sodium chloride combined does so much good is due in a large degree to the resulting addition of  $\text{Na}^+$ . If this is not added the animals will lose the fluid as fast as it is given to them. To explain the tendency to alkalosis, one must further assume that more  $\text{Cl}^-$  is lost than  $\text{Na}^+$ . If they were lost in equal amounts there would not be any disturbance of the acid-base ratio. Possibly the  $\text{Cl}^-$  is lost as hydrochloric acid and sodium chloride, while the  $\text{Na}^+$  is only lost in the latter combination.

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78. Portis, M. M., and Portis, B.: Experimental High Obstruction, *J. A. M. A.* 85:574 (Aug. 22) 1925.

79. Gamble, J. L.; Blackfan, K. D., and Hamilton, B.: A Study of the Diuretic Effect of Acid Producing Salts, *J. Clin. Invest.* 1:359, 1925. Gamble, J. L., and McIver, M. A.: A Study of the Effects of Pyloric Obstruction in Rabbits, *ibid.* 1:531, 1925. Gamble and Ross (footnote 67). Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, *J. Biol. Chem.* 57: 633, 1923.

of the fluid in the stomach and upper intestine of animals that had died without vomiting. In addition, they observed low amounts of blood chlorides in animals that had both ureters ligated. In this condition, vomiting is a marked and frequent symptom. These observations have been confirmed in substance by Brown, Eusterman, Hartman and Rowntree,<sup>12</sup> Gamble and Ross,<sup>67</sup> Ingvaldsen, Whipple, Bauman and Smith,<sup>8</sup> and White and Bridge.<sup>77</sup>

*Question 8.*—Why does the carbon dioxide combining power of the blood increase?

As is well known, a disturbance in the carbon dioxide combining power of the blood is an indication of a disturbance of the acid-base regulating mechanism of the body. The carbonic acid concentration of the blood is the most easily regulated of all the factors concerned in this relationship. The acid forming elements in the normal blood are composed of the following factors in approximately the proportions stated:  $\text{HCO}_3^-$ , 20 per cent;  $\text{Cl}^-$ , 50 per cent;  $\text{HPO}_4^{=}$ , 3 per cent;  $\text{SO}_4^{=}$ , 1 per cent; organic acids, 1 per cent; unknown acid (probably protein), 25 per cent. These figures are only approximate. The amount of  $\text{HCO}_3^-$  is the most easily adjustable and is regulated through the respiration. Therefore, if for one reason or another there is a loss of acid forming radicals from the body, this loss is made up by a retention of carbon dioxide and a subsequent rise in the  $\text{HCO}_3^-$ , which keeps the acidity of the blood at the proper level. It has already been demonstrated that there is a great loss of  $\text{Cl}^-$  from the body. Therefore, it seems safe to assume that the carbon dioxide combining power of the blood increases to compensate for this loss. If this loss of acid goes on so rapidly or to such an extent that the increase in  $\text{HCO}_3^-$ , and other acid elements can not keep up with it, there is a resulting alkalosis. This is further borne out by the fact that many patients and experimental animals show symptoms akin to tetany, which, it has been frequently proved, results from alkalosis. These symptoms are hyperexcitability and tremor. This idea was first formulated by MacCallum, Lintz, Vermilye, Leggett and Boas<sup>60</sup> and offered as an explanation of gastric tetany. McCann and Hastings, Murray and Murray<sup>75</sup> were the first to demonstrate the high carbon dioxide combining power of the blood in obstruction. This is further concurred in by Brown, Eusterman, Hartman and Rowntree,<sup>12</sup> Gamble and Ross<sup>67</sup> and others.

Some even go so far as to suggest that this disturbance in the acid-base adjusting mechanism is the overwhelming factor in the toxic picture of high obstruction (Gamble and Ross,<sup>67</sup> White and Bridge<sup>77</sup>).

77. White, J. C., and Bridge, E. H.: Loss of Chloride and Water from the Tissues and Blood in Acute High Intestinal Obstruction, Boston M. & S. J. 196: 893, 1927.

In view of what has already been discussed and from a careful comparison of the conditions, I think that one is justified in concluding that there are two conditions involved in intestinal obstruction in its broadest sense. These are: (1) Dehydration and an accompanying profound disturbance in the acid-base regulating mechanism; (2) an overwhelming toxemia.

If the problem is approached from this angle, one sees that the first process is most prominent in simple obstruction.

In experiments with closed loops both processes are at work at the same time to varying extents. If death occurs early, it is usually due to toxemia. If the animal survives for a while and vomits a good deal, dehydration and the accompanying disturbance in acid-base regulation again occur.

In strangulation, toxemia has the upper hand. The animal is overwhelmed and dies before he has a chance to become dehydrated.

The only change in the blood chemistry observed frequently in toxemia is an increase in the amount of urea.

The differences in these two conditions have been recognized by many workers (Foster and Hausler,<sup>82</sup> Gatch, Trusler and Ayers,<sup>25</sup> Hartwell and Hoguet,<sup>72</sup> Howell,<sup>28</sup> Murphy and Brooks,<sup>16</sup> and Wilkie<sup>51</sup>). Foster and Hausler<sup>26</sup> and Gatch, Trusler and Ayers<sup>25</sup> demonstrated the fact that the administration of water and sodium chloride was of no benefit in the treatment of strangulation. There are no conflicting opinions on this point.

If toxemia is present, what does it come from? The first answer that suggests itself is that it originates from the stagnating contents of the intestinal tract which have already been demonstrated to be highly toxic. The first man to suggest the possibility of toxic absorption from the intestinal tract was Amussat<sup>83</sup> in 1838. He treated a Monsieur Broussais who had carcinoma of the rectum which finally caused complete obstruction. He described the symptoms and downward course in great detail and suggested that death was due to absorption from the retained fecal matter. Bouchard,<sup>84</sup> in 1885, really sponsored the theory and was responsible for its great popularity. At one time physicians were inclined to ascribe all ills to toxic absorption from the intestinal tract. Gaspard (1822), Panum (1856), Hemmer (1866)

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82. Foster and Hausler (footnote 26); Studies of Acute Intestinal Obstruction: I. Different Types of Obstruction Produced under Local Anesthesia, *Arch. Int. Med.* 34:97 (July) 1924.

83. Amussat, J. Z.: *La maladie de Broussais, suivie de quelques réflexions pratiques sur les obstructions du rectum*, Épernay, 1845.

84. Bouchard, C.: *Lectures on Auto-intoxication in Disease*, Philadelphia, 1906. tr. French ed., 1887.

This contention of Gamble is further borne out in the experimental field by the following:

1. Gamble and Ross<sup>67</sup> were unable to prolong the lives of obstructed animals by making up the water loss with 5 per cent dextrose or ammonium chloride. All animals thus treated showed dehydration and the typical blood changes.

2. Haden and Orr<sup>80</sup> found the same result when they attempted to make up the loss of water with solutions of KCl, NH<sub>4</sub>Cl, CaCl<sub>2</sub> or MgCl instead of NaCl.

3. Haden and Orr<sup>81</sup> found that dogs with obstruction in whom the loss of fluid was made up by distilled water died more quickly than if they were untreated.

4. Gatch, Trusler and Ayers<sup>25</sup> found that normal dogs without obstruction died in six days if they were given daily clyses of distilled water.

Before leaving this subject, it is well to state that all those who claim that death in high obstruction is due totally to dehydration and alkalosis, have to explain why death in closed loops and strangulation can intervene without any evidence of either phenomenon.

*Question 9.*—Why do urinary changes occur?

The urine is scanty as a result of dehydration.

The slight trace of albumin may be taken as an indication of slight kidney damage.

The increase in the nonprotein nitrogen excretion can be taken as the result of the excess amount circulating in the blood.

The low amount chloride excretion can be taken as an index of the decreased amount circulating in the blood.

The presence of phenol and indican suggests the fact that there may be some absorption from the intestine above the obstruction. These substances are products of protein putrefaction and are present in the intestinal content. Their presence in the urine was shown by Borszesky and Genersich<sup>56</sup> and Kukula.<sup>46</sup>

It should again be emphasized that there is no evidence of marked kidney damage.

*Question 10.*—Does the pathologic picture throw any light on the subject?

This question will be taken up and discussed in later connections. It is of but little assistance.

*Question 11.*—What deductions can one draw from the different pictures presented by simple obstruction, closed loops and strangulation?

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80. Haden and Orr (footnote 70, seventh reference).

81. Haden and Orr (footnote 70, fourth reference).



days. Before using the substance, they heated the mixture to 60 C. for thirty minutes and then centrifugalized and filtered it.

Whipple and his co-workers<sup>88</sup> heated the fresh contents to 60 C. for several hours. Then they centrifugalized and filtered the substance. Occasionally, they would allow it to autolyze with chloroform and toluene for several days.

Ellis<sup>30</sup> precipitated the substance with five volumes of 95 per cent alcohol. He extracted the precipitate with boiling water to which magnesium sulphate was added to salt out the protein. The subsequent filtrate was reprecipitated with five volumes of alcohol and then filtered. This precipitate, when dried, formed a fine white powder which he dissolved in water and dialyzed against distilled water (to remove the magnesium sulphate) before using. All these methods fully demonstrated a toxic property. The difficulty is in detoxifying it rather than in demonstrating its presence.

*Question 14.*—What are the chemical properties of this toxin?

There is not entire agreement concerning these properties, but from a survey of the literature, the following facts stand out:

- (1) The toxin is held back by an earthen, but not by a paper, filter.<sup>89</sup>
- (2) It does not pass through a collodion membrane.<sup>90</sup>
- (3) It is not destroyed by boiling.<sup>91</sup>
- (4) It is not destroyed by pancreatic digestion for seven days.<sup>7</sup>
- (5) It is not destroyed by autolysis with intestinal mucosa for months.<sup>92</sup>
- (6) It is not destroyed by erepsin.<sup>93</sup>
- (7) It is probably destroyed by hydrolysis with 5 per cent sulphuric acid for six hours at 100 C.<sup>7</sup>
- (8) Repeated precipitation removes its toxicity.<sup>92</sup>

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88. Stone; Bernheim and Whipple (footnote 7). Whipple; Cooke and Stearns (footnote 59).

89. Werelius, A.: Is Death in High Intestinal Obstruction Due to Liver Insufficiency? *J. A. M. A.* 79:535 (Aug. 12) 1922.

90. Dragsted; Dragstedt and Chase (footnote 73). Whipple and Cooke (footnote 34). Whipple, G. H.; Rodenbaugh, F. H., and Kilgore, A. R.: V. Proteose Intoxication, *J. Exper. Med.* 23:123, 1916.

91. Cannon, P. R.; Dragstedt, L. R., and Dragstedt, C. A.: Intestinal Obstruction: A Study of the Influence of the Bacterial Flora on the Toxemia of Acute Obstruction, *J. Infect. Dis.* 27:139, 1920. Murphy and Brooks (footnote 16). Sugito (footnote 6). Whipple, G. H.: Intestinal Obstruction: A Proteose Intoxication, *J. A. M. A.* 65:476 (Aug. 7) 1915.

92. Charrin and Le Play: *Travaux originaux: Le rôle pathologique des poisons de l'intestin*, *Semaine méd.* 24:377, 1904. Whipple (footnote 91, fourth reference).

93. Whipple, G. H., and Van Slyke, D. D.: Proteose Intoxication and Injury to Body Protein: III. Toxic Protein Catabolism and its Influence on the Non-Protein Nitrogen of the Blood, *J. Exper. Med.* 28:213, 1918.

and Bergmann and Schmeideberg (1868) (quoted from Bouchard <sup>84</sup>) demonstrated that various products of putrefaction were highly toxic when injected into animals. Bouchard killed rabbits by injections of macerated muscle extract. He felt that there were four sources of intestinal auto-intoxication:

- (1) Food.
- (2) Bile.
- (3) Putrefaction of alimentary residues.
- (4) Fecal matter—mostly due to certain salts of potassium and ammonia.

*Question 12.*—What, then, is this toxic substance that is found in the intestinal content above an obstruction?

The answer to this question is not clear. The problem should be considered from different sides and then, if possible, conclusions reached.

One thing that should be borne in mind is that the toxin can be formed in a closed loop with almost unbelievable rapidity. Bunting and Jones <sup>14</sup> isolated it from the lumen of the bowel three hours after simple obstruction:

*Question 13.*—How must the content above an obstruction be prepared in order to demonstrate its toxic properties?

Murphy, Brooks and his co-workers <sup>85</sup> did not prepare it. They simply took the fluid content above an obstruction and used it for injections. Sometimes they strained it, and at other times they diluted it with an equal amount of distilled water.

Clairmont and Ranzi <sup>86</sup> filtered the contents through a Chamberland filter before injection.

Dragstedt, Dragstedt and co-workers <sup>80</sup> strained the fluid and heated it for one hour at 70 C. The coagulum was then filtered off, and the filtrate was kept with chloroform and toluene until needed for injection. Before using the substance, the preservatives were removed by heating and filtering.

Davis and Morgan <sup>87</sup> took the mucosa with the fluid. Then they mixed this with physiologic sodium chloride, added toluene and chloroform and allowed the mixture to autolyze at 37 C. for from two to ten

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85. Copher and Brooks (footnote 23). Murphy and Brooks (footnote 16). Murphy and Vincent (footnote 29).

86. Dragstedt, C. A.; Dragstedt, L. R., and Chase.: The Antigenic Property of Closed Intestinal Loop Fluid, *Am. J. Physiol.* 46:366, 1918.

87. Davis, D. M., and Morgan, H. S.: Natural Immunity of Animals Against Poison of Intestinal Obstruction, *Bull. Johns Hopkins Hosp.* 25:39, 1914.

toxicity: Proteoses, heteroproteoses, deuteroproteoses, protoproteoses, putrescin, cadaverine, histamine, choline, neurine and muscarine.<sup>97</sup>

Kukula<sup>40</sup> concluded that none of these existed in the intestine in sufficient quantities or were absorbed to a great enough extent to cause death.

It must be remembered that this is an extremely complicated field and that there probably exist in the intestine many substances that have not as yet been isolated.

*Question 16.*—What other substances does this toxic material resemble in its action?

In 1822, Gaspard (quoted from Bouchard<sup>84</sup>) found that if he injected extracts of putrid meat into experimental animals the resulting symptom complex and a pathologic picture were almost identical with those described for the injection of contents after obstruction. He is the first man to describe the hyperemia of the upper intestinal tract so characteristic of these conditions.

In 1856, Panum (quoted from Bouchard<sup>84</sup>) described the same thing. However, he took the precaution to boil his putrid extract before injection. He also found that the toxic factor could be precipitated by alcohol.

Whipple and co-workers<sup>95</sup> and Chittenden, Mendel and Henderson<sup>100</sup> brought out the striking similarity between the pharmacologic actions of the toxic substance and proteose as evidenced by marked fall in blood pressure, prolonged coagulation time and the increased flow and reduced coagulability of the lymph.

Stone<sup>37</sup> and Gerard<sup>90</sup> showed that the action of the toxin is almost identical with that of histamine.

Barger and Dale<sup>101</sup> described a symptom complex common to the pharmacologic actions of commercial peptone, extracts of intestines, thyroid, brain, etc., and of histamine which consists of vomiting, purging, salivation, labored respiration, low blood pressure, collapse and death. Histamine differs from the others in that it does not cause a loss of coagulation of the blood while the others do.

Whipple and his co-workers<sup>102</sup> brought out the similarity of the action of the toxin to the reactions seen in conjunction with large overdoses of epinephrine and fatal anaphylactic shock. South and Hardt<sup>12</sup> also emphasized the similarity of anaphylaxis. This will be taken up later.

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100. Chittenden, R. H.; Mendel, L. B., and Henderson, Y.: Chemico-Physiological Study of Certain Derivatives of the Proteids, *Am. J. Physiol.* 2:142, 1898-1899.

101. Barger, G., and Dale, H. H.:  $\beta$ -Iminazolyethylamine, a Depressor Constituent of Intestinal Mucosa, *J. Physiol.* 41:499, 1910-1911.

102. Whipple: Rodenbaugh and Kilgore (footnote 90, third reference).

(9) It loses its toxicity if dialyzed against physiologic sodium chloride for several hours.<sup>94</sup>

(10) It loses its toxicity by repeated filtration.<sup>95</sup>

(11) It loses its toxicity by long standing in the icebox.<sup>95</sup>

(12) It is soluble in water.<sup>94</sup>

(13) It is thrown out of solution rich in albumin by boiling.<sup>95</sup>

(14) It is precipitated by five volumes of alcohol.<sup>96</sup>

(15) It is precipitated by albumin.<sup>6</sup>

(16) It is precipitated by 60 per cent ammonium sulphate.<sup>6</sup>

(17) It does not stimulate pancreatic digestion.<sup>95</sup>

*Question 15.*—What substances have been demonstrated in the intestinal tract that might contain the toxic factor?

These substances might be divided into two classes: (1) those that are products of normal digestion plus normal bacterial action, and (2) those that are the products of stagnant digestion, where the bacterial action is more marked.

The substances produced by normal digestion plus normal bacterial action are as follows: From proteins—metaproteins, proteoses, heteroproteoses, deuteroproteoses, protoproteoses, peptones, polypeptids, amino-acids, ammonia, hydrogen sulphide, nitrogen, methyl mercaptan, phenol, cresol, dioxybenzene, phenylacetic acid, phenyl propionic acid, indol, skatol, tyrosine, dioxybenzene, resorcinol, hydroquinone and pyrocatechin<sup>97</sup>; from fats and lecithins—oxycholesterol, fatty acids, glycerol phosphoric acid, choline, neurine and muscarine<sup>98</sup>; from carbohydrates—derivatives of glucosamines and mucin, water, carbon dioxide and various disaccharids and polysaccharids.<sup>99</sup>

Stagnant digestion plus bacterial action, in addition to all of the fore-mentioned substances, produces the following: Pyridine, chinoline, toxalbumins, ptomaines, diamines, tetramethyldiamine (putrescin), pentamethyldiamine (cadaverine), ethyldiamine and histamine.<sup>44</sup>

These products probably owe their existence to much increased bacterial action. From the foregoing list the following have a known

94. Ellis (footnote 36). Whipple (footnote 91, fourth reference).

95. Whipple (footnote 91, fourth reference).

96. Ellis (footnote 36). Sugito (footnote 6). Werelius (footnote 89). Whipple (footnote 91, fourth reference).

97. Schloss, quoted by Gerard, R. W.: The Lethal Agent in Acute Intestinal Obstruction, *J. A. M. A.* 79:1581 (Nov. 24) 1922. Kukula (footnote 46). Nesbitt, B.: On the Presence of Cholin and Neurin in the Intestinal Canal During its Complete Obstruction: A Research on Auto-Intoxication, *Dominion M. Month.* 12:113, 1899. Sweet; Peet and Hendrix (footnote 22, second reference).

98. Gerard (footnote 97, first reference). Sweet; Peet and Hendrix (footnote 22, second reference).

99. Gerard (footnote 97, first reference).

their results look convincing, many other experimenters have tried and failed to show any signs of immunity (Brooks<sup>20</sup>; Dragstedt, Dragstedt and co-workers,<sup>106</sup> Davis and Morgan,<sup>87</sup> Ellis,<sup>36</sup> Magnus-Alsleben<sup>104</sup> and others). It seems as if Whipple's results along this line would have to be laid to normal variation.

Wilkie<sup>19</sup> also thought the substance a proteose.

Sweet,<sup>107</sup> Eisberg<sup>6</sup> and Schönbauer<sup>108</sup> ventured the opinion that it is a protein split product related in some way to the toxic proteoses. Sweet mentioned the possibility of the substance being attached to the proteose molecule rather than its being the proteose itself. This is borne out by the fact that the toxicity is lost by repeated filtration or precipitation.

Schönbauer<sup>108</sup> felt that it is a product of tryptic fermentation of albuminous decomposition products. He even went so far as to state that it is trypsin itself, which he believed is closely related in chemical composition to the protein split products. He reported the presence of trypsin in the peritoneum of dogs dying from high obstruction. He also reported beneficial results in high obstruction when injections of serum having a high antitryptic titer were given. He found the serum of diabetic persons to have this quality.

Stone<sup>57</sup> and Gerard<sup>60</sup> felt that it is histamine or a histamine-like product.

Wangensteen and Loucks,<sup>109</sup> working with histamine injections into the lumen of the bowel, could not obtain evidence of its absorption by normal, obstructed or distended gut.

Dragstedt, Dragstedt and co-workers<sup>110</sup> felt that it is related in some way to the toxic amines.

Eisberg and Draper<sup>111</sup> offered the suggestion that it is a substance of biochemical origin similar to parathyroid or other endocrine secretions.

106. Cannon; Dragstedt and Dragstedt (footnote 91, first reference). Dragstedt; Dragstedt and Chase (footnote 73). Dragstedt, C. A., and Moorhead, J. J.: *Immunity in Intestinal Obstruction*, J. Exper. Med. 27:359, 1918.

107. Sweet (footnote 22, first reference, and footnote 38).

108. Schönbauer (footnote 33). Schönbauer (footnote 33). Schönbauer, L., and Löffler, E.: *Ueber Ileuserum: Experimentelle und klinische Untersuchungen*. Wien. klin. Wchnschr. 38:135, 1925.

109. Wangenstein, O. H., and Loucks, M.: *Studies in Intestinal Obstruction: II. The Absorption of Histamine from the Obstructed Bowel*, Arch. Surg. 16: 1089 (May) 1928.

110. Dragstedt; Dragstedt, and Chase (footnote 86). Dragstedt; Dragstedt; McClintock, and Chase (footnote 15). Dragstedt and Moorhead (footnote 106, third reference).

111. Eisberg, H. B., and Draper, J. W.: *Intestinal Obstruction: Continued Studies*, J. A. M. A. 71:1634 (Nov. 16) 1918.

*Question 17.*—What other conditions will cause the production of the toxin?

First of all, it has already been stated that the toxin can be recovered from the intestinal lumen of animals that have themselves been killed by toxic injection. Ellis<sup>30</sup> emphasized the fact that this makes its appearance with almost unbelievable rapidity. He produced a duodenal fistula in a dog and then subjected the animal to toxic injection. He collected duodenal contents before and after injection, and found that they almost immediately became toxic.

Gurd<sup>103</sup> found the intestinal contents toxic in a dog that had been killed by tying off the portal vein.

Magnus-Alsleben<sup>104</sup> described a strong toxicity of the intestinal content of dogs following a meat diet.

Ellis<sup>30</sup> described toxicity of the intestinal contents in dogs that have died from the following conditions: Thrombosed Eck fistula, distemper, acute pancreatitis, sterile peritonitis produced by dropping a piece of fresh pancreas into the abdominal cavity and bilateral supra-renalectomy.

*Question 18.*—What, then, is this toxin?

It has already been stated that it is not known what it is. The best that can be done is to quote the various opinions that have been expressed in the literature.

Whipple and his co-workers<sup>105</sup> thought that it is a proteose because it has the following properties in common with a proteose:

- (1) Both are thrown out of a solution rich in albumin by boiling.
- (2) Both are nondialyzable.
- (3) Neither is destroyed by pancreatic digestion.
- (4) Both are precipitated by alcohol and soluble in water.
- (5) Both present the same clinical and pathologic picture when injected.
- (6) Injection of both causes a rise of nonprotein nitrogen in the blood.
- (7) Dogs are highly susceptible to both, while cats and rabbits are not.

However, dogs can not be immunized to toxic injection. Whipple and his co-workers performed a long series of experiments which seemed to show that dogs could be immunized to toxic injection and that by means of repeated sublethal doses of the toxin they could be made relatively immune to subsequent obstruction. However, although

103. Gurd in Maury (footnote 1, first reference).

104. Magnus-Alsleben, E.: Ueber die Giftigkeit des normalen Darminhalts. *Beiträge z. chem. Physiol. u. Path.* 6:503, 1904.

105. Stone, H. B.; Bernheim, B. M. and Whipple, G. F.: The Experimental Study of Intestinal Obstruction. *Ann. Surg.* 59:714, 1914. Whipple (footnote 91, second reference). Whipple; Rodenbaugh and Klinger (footnote 92, third reference).

This has not been confirmed by any subsequent observation. Ellis<sup>36</sup> found gastric contents nontoxic. Stone<sup>37</sup> felt that the toxin was not formed in the stomach. Many other workers agree. It looks as if Roger and Garnier's observations would again have to be attributed to normal variation. The general opinion is that the stomach is not the source.

*Question 21.*—Does the toxin come from the biliary tract?

Bouchard<sup>84</sup> reported that normal bile is toxic. However, it is easy technically to eliminate the excretion of bile from the gastro-intestinal tract and then produce obstruction in the animal, thus ruling out the bile. This experiment has been performed repeatedly by many workers who come to the universal conclusion that the elimination of the bile does not influence the picture (Bunting and Jones,<sup>14</sup> Draper Maury,<sup>114</sup> McClure,<sup>115</sup> Sweet,<sup>116</sup> Stone, Bernheim and Whipple,<sup>7</sup> and others).

*Question 22.*—Does the toxin come from the pancreas?

The idea of ascribing the origin of the toxin to the pancreas is an attractive one. In the first place, the clinical pictures of high obstruction and acute pancreatitis are almost identical (Sweet<sup>117</sup>). Then, the toxin can be recovered from the intestine of an animal that has died of acute pancreatitis (Ellis<sup>36</sup>). Also, the pancreatic juice is the chief protein splitter of the body and there are those that think the toxin is a protein split product. In addition to this, pancreatic juice is itself toxic when injected after being activated. And, finally, the lethal line of Draper lies just below the opening of its duct in the dog.

In considering the evidence of the toxicity of the pancreatic secretion, the outstanding example is acute pancreatitis in which, it is believed, the enzymes become activated, find access to the blood stream and cause sudden death.

Sugito<sup>6</sup> reported that normal pancreatic secretion is not toxic. He observed, however, a rapid development of a great toxicity if he added a small number of bacteria to it. Cybulski and Tarchanoff<sup>43</sup> reported a toxicity of pure pancreatic juice which, however, becomes greatly enhanced by putrefaction. They stated that its injection lowers the blood pressure, increases the rate of respiration and abolishes the

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114. Maury, J. W. D.: Intestinal Obstruction: An Outline for Treatment Based upon the Cause of Death, *Am. J. M. Sc.* 137:725, 1909; (footnote 1, second reference).

115. McClure, R. D.: Experimental Study of Intestinal Obstruction, *J. A. M. A.* 49:1003 (Sept. 21) 1907.

116. Sweet (footnote 22, first reference).

117. Sweet, J. E.: High Intestinal Obstruction, Post-Operative Ileus and Acute Pancreatitis, *Penn. M. J.* 16:520, 1912-1913; (footnote 22).

Murphy and Vincent<sup>29</sup> and Williams<sup>9</sup> thought it is a bacterial exotoxin.

Nesbitt<sup>112</sup> thought that cholin is the toxic factor. Cholin has a curare-like action, increases intestinal movements and paralyzes the heart. This, of course, is not in accordance with the accepted picture of toxic injection. It does, however, suggest the possibility of there being more than one toxin as the cause of death.

Ingvaldsen, Whipple, Bauman and Smith<sup>8</sup> made a careful and delicate chemical analysis of the substance. After various purifying processes (which amplified the method used by Ellis<sup>30</sup>), they succeeded in isolating 1 Gm. of white powder from the combined contents of fourteen dogs with obstruction. They found that 71 mg. of this substance would kill a dog weighing 5.5 Kg., in two and three-quarters hours. After careful analysis of this substance, they decided that it was a nucleoprotein for the following reasons:

1. There was greater solubility in alkali and strong acids than in weak acids.

2. It was not coagulated by heat.

3. Chemical analyses and reactions showed that it contained phosphoric acid and a pentose.

They also demonstrated the presence of very small amounts of histamine in content obtained after obstruction. This, they felt, was not sufficient to cause symptoms.

Bouchard<sup>84</sup> thought it was an alkaloid.

Murphy and Brooks<sup>10</sup> suggested that it was a ptomaine.

I am afraid that I shall have to leave it to the reader to take his choice.

The next question to investigate is the possible origin of the toxin. Possibly some light can be thrown on the subject by investigating its source.

*Question 19.*—From what does the toxin come?

In investigating this question, it seems best to start at the beginning of the gastro-intestinal tract and to look into every possible source.

*Question 20.*—Is the toxin formed in the stomach?

The only evidence that the stomach is the elaborator of the toxin is found in the work of Roger and Garnier.<sup>113</sup> They isolated a toxic substance from the gastric mucosa which they called a gastrototoxin.

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112. Nesbitt (footnote 97, third reference).

113. Roger and Garnier (footnote 47); Note sur la toxicité des extraits préparés avec les parois du tube digestive, *Compt. rend. Soc. de biol.* 64:426, 610 and 883, 1908.



On the other hand one cannot escape the fact that depancreatized animals with obstruction die just the same and with a picture not to be distinguished from that presented by normal animals with obstruction (Bunting and Jones,<sup>14</sup> Ellis<sup>30</sup> and Sweet<sup>116</sup>). Furthermore, Ingvaldsen, Whipple, Bauman and Smith<sup>8</sup> demonstrated the presence of the toxin in the gut of depancreatized animals that had died from obstruction.

Thus the idea that toxin comes from the pancreas must be relinquished.

*Question 23.*—Does the toxin come from the intestinal mucosa?

Experimentation along these lines is immediately faced by the great difficulty of eliminating the intestinal mucosa and its influences from the experimental animal. The intestinal secretion consists of:

(1) A purely mucoid secretion from the glands of Brunner in the duodenum.

(2) Succus entericus which is made up of the following components:

(a) Enterokinase, the activating factor for the proteolytic enzyme of the pancreatic juice, converting tripsinogen to trypsin.

(b) Erepsin, which acts on the proteoses and peptones, breaking them up to amino-acids during the process of absorption. Erepsin cannot be obtained from the lumen, but is in the cells. Erepsin is also reported to exist in the liver, kidney, pancreas and other tissues. This is an important enzyme.

(c) Enzymes which act on the carbohydrates, converting polysaccharids and disaccharids to dextrose.

(d) Nuclease, which works on nucleoproteins, splitting the nucleic acid to purine and pyrimidine bases.

(e) Secretin, which stimulates pancreatic secretion.

Whipple and his co-workers<sup>121</sup> are the great champions of the intestinal mucosa as the elaborator of the toxin. They found that extracts of the mucosa of animals with obstruction contained the same toxic properties as the intestinal contents. They conceived of the toxic substance as being elaborated in the mucosa cells, some being excreted into the lumen of the gut, some remaining in the cells, and the remainder being excreted into the circulation, causing the toxic symptoms and death. In their experiments they report a toxicity of the contents coming from isolated drained loops. Building on this foundation, they constructed their theory which, in substance is as follows: The mucosa cells, they claimed, depend for their normal action on the stimulus received from the normal passage of intestinal contents. They are stroked and bathed by it and in return they produce the secretions necessary for digestion. If this process is interrupted, as it is in a simple obstruction, they suggested that the action of the cells becomes

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121. Stone: Bernheim, and Whipple (footnote 105, first reference, and footnote 42).

coagulability of the blood. Schönbauer<sup>22</sup> showed that simultaneous introduction of trypsin and bacteria into the peritoneum caused rapid death, while twice the amount of trypsin or twice the number of bacteria alone does not have any effect on the control animals. Sweet and his co-workers<sup>117</sup> found that if they put pancreatic juice or dropped a piece of fresh pancreas into a low closed ileal loop (which is normally compatible with life indefinitely), the animal became toxic and quickly died with the typical picture of high obstruction.

Further evidence of the possibility that the pancreas is the originator of the toxic substance lies in the fact that animals with simple obstruction die with maximal rapidity if that obstruction is at a point just below the entrance of the pancreatic ducts (fact 1). This was observed by Draper Maury,<sup>118</sup> Eisberg<sup>5</sup> and Sweet.<sup>119</sup> Draper Maury,<sup>118</sup> Sugito<sup>6</sup> and Eisberg<sup>5</sup> reported that life is prolonged in obstruction if, by one means or another, the pancreatic secretion is made to enter the intestinal tract aboral to the obstruction. This conclusion was drawn from a large number of experiments. Sweet and his co-workers<sup>22</sup> reported that if the pancreas is removed and high obstruction perpetrated, death will come in seven or eight days as opposed to death in two or three days if obstruction is established without the removal of the pancreas. They also expressed the opinion that obstructed depancreatized animals die with a slightly different picture. Sweet also emphasized the great similarity of the symptom complexes and pathologic pictures presented by high obstruction, acute pancreatitis and bilateral suprarenalectomy. In line with this, Sweet and Pemberton<sup>120</sup> demonstrated that injections of suprarenal and pituitary extracts have an inhibitory action on the pancreatic secretion which is independent of changes in the blood pressure.

This work is pregnant with possibilities and stimulating to the imagination. Could it be possible that absorption of activated pancreatic juice is the cause of death? And that conditions for the activation and absorption can be produced in a number of ways (i.e., by obstruction, closed loops, strangulation, bilateral suprarenalectomy, etc.)? And then, is it not possible that the toxic substance is reexcreted into the intestinal lumen, for instance, into closed loops? This idea has been toyed with by Sweet,<sup>117</sup> Draper Maury<sup>118</sup> and Eisberg. Such a conception would also explain, possibly, the extreme rapidity with which the toxin is formed as observed by Bunting and Jones.<sup>4</sup>

118. Maury (footnote 1, second reference).

119. Sweet (footnote 117, first reference).

120. Pemberton, R., and Sweet, J. E.: Further Studies on the Influence of the Ductless Glands on the Pancreas, *Arch. Int. Med.* 5:466 (May) 1910.

laparotomy was done and the loop contents were found to be sterile. The ends were then inverted and the sterile closed loops were returned to the abdomen as before. They found that animals thus treated lived indefinitely regardless of from what level the loop was taken. They further were able to strangle these loops without any deleterious effect to the animal. From this they concluded that the intestinal secretion could have nothing to do with the elaboration of the toxin.

Davis and Stone<sup>40</sup> found that normal intestinal secretion from which bacterial action had been eliminated by the addition of chloroform and toluene could be autolyzed indefinitely without becoming toxic. They claimed that this method did not stop enzyme action, and they therefore concluded that intestinal secretion did not form the toxin.

Gerard<sup>99</sup> called attention to the fact that the formation of toxin goes on in a strangulated loop, where the mucosa is largely rotted away. He offered this as evidence of the fact that intestinal mucosa cannot elaborate the toxin.

Murphy and Brooks<sup>10</sup> tied the cystic duct of dogs and found it compatible with life. They then inserted into the thus distended gall-bladder a few loopfuls of culture obtained from the intestinal contents after obstruction. These animals quickly died of the typical picture of toxemia. From this they concluded that the intestinal mucosa is not at all necessary for the elaboration of the toxin.

*Question 24.*—Is, then, the toxin the result of bacterial action? This subject has already been touched on.

Those who have tried to ascertain the rôle played by bacteria are faced by the great difficulty of eliminating them entirely from the intestinal tract. The normal intestinal tract is inhabited by great quantities of bacteria of varieties too numerous to mention—aerobes and anaerobes. The most prominent aerobes are the members of the colon bacillus family while the Welch bacillus leads the list of the anaerobes. The normal small intestine is relatively sterile, especially in its upper reaches. The growth becomes more populous near the ileocecal valve, and is tremendous in the colon which is the happy hunting ground for bacteria. It is a well known fact that the intestinal content of any animal that has died from high obstruction, closed loop or strangulation is rich in bacteria no matter where the obstruction exists. What is the significance of this fact?

There is good evidence to prove that normal intestinal content, if incubated presumably to promote bacterial activity, will develop toxic properties in a relatively short time. This has been nicely proved by Davis and Stone,<sup>40</sup> Murphy and his co-workers<sup>124</sup> and Sugito.<sup>6</sup> Fur-

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124. Murphy and Brooks (footnote 16). Murphy and Vincent (footnote 29).

perverted and instead they produce a poisonous substance. Their technique in their fundamental experiment was, however, open to criticism. As was pointed out by Sweet,<sup>22</sup> they made many of their isolated drained loops by double ligature of the duodenum and gastro-enterostomy distal to the second ligature. This, therefore, did not eliminate the possibility of there being a functional obstruction above the first ligature in the stump of the duodenum. Therefore, they could not claim that the toxin was not formed in this stump and reexcreted into the drained loop. Also, it must not be forgotten that drained loops are frequently compatible with life, and that a toxicity can sometimes be demonstrated in normal intestinal content.

Draper and his co-workers,<sup>122</sup> after experiments on over 400 animals, concluded that the toxin is a normal product of the duodenum related to the gastrot toxins of Roger and Garnier.<sup>47</sup> This substance, they felt, is normally neutralized lower in the intestinal tract. When an obstruction intervenes, however, the toxin is not detoxified, but is absorbed unchanged and causes death. This would seem to explain the greater fatality of high obstruction, because if the obstruction were lower there would be varying degrees of detoxication and a resultant prolongation of life. Ellis<sup>26</sup> also concurred in this theory to a certain extent. Draper and his co-workers tried to develop this theory into a therapeutic advantage by feeding the jejunal and ileal mucosa of normal animals to animals with obstruction with the idea of detoxifying the fluid produced by the obstruction. At first they reported beneficial results, but were later forced to retract their statement.

Schönbauer<sup>23</sup> felt that trypsin is the offending substance and described its presence in the Brunner glands of the duodenum. He thought that it becomes activated and forms a protein split product which is absorbed and causes the toxic picture.

Bunting and Jones<sup>24</sup> thought that the toxin is formed in the duodenum.

Hartwell<sup>123</sup> suggested that it is elaborated by the injured mucosa.

Others have tried to eliminate the mucosa from the picture as follows:

Dragstedt and his co-workers<sup>4</sup> isolated segments of intestine and left them open in the peritoneal cavity with all nerves and vascular elements intact. These animals remained well. At a later date another

122. Maury (footnote 114, first reference; and footnote 1, second reference): Draper, J. W.: *Experimental Intestinal Obstruction: Report of Further Physiologic, Cytologic and Chemical Studies*, J. A. M. A. 57:1338 (Oct. 21) 1911; footnote 10; *Intestinal Obstruction*, *ibid.* 67:1080 (Oct. 7) 1916. Eisberg and Draper (footnote 111).

123. Hartwell (footnote 27, first reference).

in all cases of the toxemia of high obstruction. Largely as a result of this work, many other investigators were swung around to this opinion (Gerard,<sup>90</sup> Gurd,<sup>129</sup> South and Hardt,<sup>13</sup> Wilkie,<sup>19</sup> and others). Stone<sup>37</sup> claimed that histamine was formed by bacterial action and suggested that it was the cause of death.

If it is due to bacterial action, what bacteria are responsible? Clairmont and Ranzi,<sup>29</sup> after considerable experimentation, expressed the opinion that the aerobic bacteria, rather than the anaerobes, were responsible. Scholefield<sup>32</sup> favored the anaerobes, especially *B. welchii*.

Williams<sup>9</sup> did a careful and interesting piece of work on this subject. He quoted the report of the Committee on Anaerobic Bacteria which functioned during the World War. They give the following description of the toxemia associated with gas gangrene: "Vomiting is frequent. The pulse is rapid. The extremities are cold and blue. The temperature falls. The mind stays acute to the end. In the terminal stages some degree of icterus may be present." He noticed the marked resemblance between this picture and that of toxemia in high obstruction. Therefore he studied the Welch bacillus as the elaborator of the toxin producing death.

He observed that the Welch bacillus was by far the commonest anaerobe in the intestinal tract. He isolated it from the vomitus and intestinal content after obstruction in a high percentage of cases of ileus.

He studied the conditions necessary for its growth and production of toxin. He found that it needed a neutral or slightly acid medium. This, he found, was provided in the small intestine, especially the terminal ileum. In the colon, where the medium is acid, he found but few living organisms of this species.

He next tried to prove that the toxic substance in intestinal material after obstruction was Welch bacillus toxin. Accordingly, he made injections into two series of mice, one with the contents after obstruction and the other with the contents plus Welch bacillus antitoxin. He found that in the first series of mice, 50 per cent died, whereas in the second they all lived. As further evidences of the absorption of Welch bacillus toxin, he noted fatty degeneration of the heart and liver and hemolytic staining of the intima of the arteries of patients dying from obstruction. This is also found in patients dying from gas gangrene. He stated that he was unable to demonstrate the presence of gas bubbles in the liver which, of course, is an outstanding feature in patients overwhelmed with gas bacillus infection, but is not an essential to his theory of toxin absorption from the intestine.

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129. Gurd, F. B.: The Toxins of Intestinal Obstruction, *J. Infect. Dis.* 15:124. 1914.

thermore, Davis and Stone showed that normal contents do not develop toxicity as long as bacterial action is eliminated. Albu<sup>125</sup> and Bouchard<sup>84</sup> also thought that the toxin is the result of putrefaction, comparing the pharmacologic action to that of putrid meat.

On the other hand, Whipple and his co-workers<sup>42</sup> stated that normal mucosa extract putrefied and antolyzed did not produce toxicity. Roger and Garnier<sup>126</sup> also felt that putrefaction has little to do with it.

From the application of this to the experimental field, the following is found:

Zimmerman<sup>127</sup> reported two cases of infants born with congenital atresia of the small intestine. They died without showing signs of toxemia. He attributed this to the absence of organisms in their intestinal tract.

Albeck<sup>45</sup> did a very interesting experiment. He observed the fact that the intestinal tracts of hibernating animals are sterile. Therefore, he strangulated 20 cm. of the small intestine of a hibernating hedge hog. The animal did not wake up until the second day when it drank some milk. Death occurred on the sixth day. He was inclined to attribute the death to the fact that it introduced bacteria into its intestinal tract by drinking the milk and the resultant putrefaction.

Dragstedt, Dragstedt and co-workers<sup>128</sup> tried many methods of sterilizing a closed loop. They found that if they washed out the loop with ether before closing, a large proportion of dogs lived regardless of the level of the loop. At postmortem examination, however, they found bacteria in small numbers in these loops. They attributed this survival to some astringent action of the ether on the intestinal mucosa which reduced its permeability. They obtained the same results with tannic acid.

Their experiments by which they could sterilize loops by leaving them open in the peritoneal cavity have already been described. From these experiments, they concluded that health was not compromised in obstruction in the absence of bacteria, and that therefore microorganisms elaborated the toxin. Murphy and Brooks<sup>16</sup> did the same experiments with similar results. These workers took this to be final proof that bacteria elaborated the toxin and had, therefore, to be present

125. Albu, A.: *Die Autointoxicationen des Intestinaltractus*, Berlin, 1895, chapter 1, pp. 16-23.

126. Roger, H., and Garnier, M.: *Nouvelles recherches sur les poisons intestinaux*, *Rev. de méd.* 30:233, 1910.

127. Zimmerman, H. B.: *Acute Intestinal Ileus*, *Minnesota Med.* 5:156, 1922.

128. Dragstedt; Dragstedt; McClintock, and Chase (footnote 31, first reference; and footnote 15, first reference); Dragstedt and Moorhead (footnote 106, third reference). Dragstedt; Moorhead. and Burcky (footnote 41, second reference; and footnote 4).

4. Why does the toxin appear in cases in which there is no reason to suspect stagnation of intestinal contents? It is reported in acute pancreatitis, thrombosis of the portal vein, bilateral suprarenalectomy and distemper.<sup>36</sup>

Whipple and his co-workers<sup>131</sup> were unable to eliminate bacteria, but felt that they were ruled out for some of the foregoing reasons and also because with a closed washed loop there are symptoms which result in death, whereas postmortem examination shows very few organisms in the loop. Buchholz and Lange<sup>132</sup> were able to diminish the numbers of bacteria and completely avert their development by feeding acriflavine before obstruction. They reported that it did not influence the picture. Schönbauer<sup>33</sup> felt that bacteria were ruled out because strangulation of the colon is much less fatal than strangulation of the small intestine. Roger and Garnier<sup>128</sup> felt that putrefaction had little to do with the picture.

*Question 25.*—Does the toxin arise from partly digested food?

It is safe to assume that it does not arise solely from partly digested food. Most experimenters have taken the precaution of starving their animals before producing obstruction, thus eliminating this variable. There are, however, some interesting side-lights that suggest that food may increase the amount of toxin and cause its formation in normal gut. In the first place, it has already been demonstrated that certain products of normal digestion are toxic.

Roger and Garnier<sup>133</sup> found that the intestinal contents were nine times more toxic after a meat diet than after a milk diet.

Magnus-Alsleben<sup>104</sup> found the normal contents toxic after every kind of food but milk.

Wilkie<sup>131</sup> found that dogs died much more quickly from strangulation, if it was preceded by a protein diet.

Cannon, Dragstedt and Dragstedt<sup>134</sup> found proteolytic bacteria common in the intestinal tract, but were unable to eliminate them by any kind of diet.

This work would seem to add weight to the argument that the toxin is derived from protein digestion.

All the available evidence of the existence and formation of a toxin in the lumen of the obstructed intestine having been reviewed, the fol-

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131. Stone; Bernheim, and Whipple (footnote 7; footnote 105, first reference, and footnote 42).

132. Buchholz, W., and Lange, H.: Ileus and Darmflora, *München med. Wehnschr.* 74:233, 1927.

133. Roger, H., and Garnier, M.: Influence du régime lacté sur la toxicité du content intestinal, *Compt. rend. Soc. de biol.* 59:677, 1905; footnote 126.

134. Cannon; Dragstedt, and Dragstedt (footnote 91, first reference).

He then applied the therapeutic test by treating patients suffering from acute appendicitis at St. Thomas' Hospital in London. He chose acute appendicitis, because it was fairly common, because the condition gives fair warning of various complications before these complications develop to the fullest extent, and because the mortality in the disease was well established (6.5 per cent at St. Thomas' Hospital). He gave the antitoxin in eighteen of 256 unselected cases in which, in the opinion of consultants, the chances of life were 50 per cent or worse. In this series, he had a mortality rate of 1.17 per cent. In a series of 111 control cases in the hospital at the same time, and in which antitoxin was not administered, the mortality rate was 6.3 per cent.

Also, in fifty-four cases of acute obstruction from one cause or another, he gave treatment in nineteen with five deaths. He quoted the mortality rate in these cases as being 9.3 per cent. He opposed this to 214 cases in the hospital from 1919 to 1923, in which treatment with antitoxin was not given, as being 24.8 per cent.

He reported an immediate and striking improvement in the patients as soon as they receive the treatment.

This seems rather convincing, but a closer study of the facts reveals certain weaknesses. In the first place, Welch bacillus toxin is extremely labile, being easily destroyed by heat and slight changes in acidity. The toxin generally conceded to be present in the obstruction material is stable, not even being touched by boiling. In the second place, it was unfortunate that he chose acute appendicitis for his therapeutic test, because there is an added factor of infection which might well be due in some degree to the Welch bacillus. Finally, his statistics on the treatment of pure high obstruction would be more convincing if he compared his percentage mortality in the cases in which treatment was given with the percentage mortalities in his control cases divided into groups of fifty-four consecutive admissions.

All those who claim that bacteria elaborate the toxin must answer the following questions:

1. Why is it that high obstruction is so much more fatal than low obstruction when the low small intestine contains many more bacteria than the upper? <sup>130</sup>

2. Why does the toxin appear so rapidly after obstruction? Bunting and Jones<sup>14</sup> reported its appearance in three hours after duodenal obstruction.

3. Why does the toxin reappear with such rapidity in the intestine of dogs that have received injections of it? Ellis<sup>36</sup> reported that it appears almost immediately.

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130. Draper (footnote 122, fifth reference). Stone; Bernheim, and Whipple (footnote 7). Werelius (footnote 89).



The majority of workers believe that they are the same picture (Dragstedt, Dragstedt and co-workers,<sup>136</sup> Stone,<sup>37</sup> Whipple and his co-workers<sup>137</sup> and many others).

Braun and Boruttau,<sup>40</sup> Foster and Hausler,<sup>71</sup> Hartwell and his co-workers,<sup>11</sup> South and Hardt<sup>13</sup> and Werelius<sup>89</sup> think that the two pictures do not bear enough similarity to be due to the same process.

Again, the reader will have to take his choice. Perhaps more light can be thrown on the subject by what follows.

*Question 27.*—What evidence is there that a toxin is absorbed?

In the first place, an animal may live for a long time with a closed loop which contains many times the lethal dose of toxin. This has been often proved (Dragstedt, Dragstedt and co-workers,<sup>138</sup> Murphy and Brooks,<sup>10</sup> Whipple and his co-workers<sup>7</sup> and others).

McLean and Andries,<sup>139</sup> Werelius<sup>89</sup> and Clairmont and Ranzi<sup>39</sup> tried transfusing the entire blood content from a toxic animal with obstruction into a normal animal. They did not obtain any toxic effect.

Whipple and his co-workers gave a dog a large enough dose of toxin to produce marked symptoms. In two hours they transfused his whole volume of blood into a normal animal, without an unfavorable effect. This would indicate that the toxin is taken up rapidly and held somewhere outside the blood stream. It further suggests that the fact that toxin cannot be demonstrated in the blood would not necessarily mean that it was not absorbed.

Murphy and Brooks<sup>10</sup> did the following interesting experiment: They placed a cannula in the thoracic duct of a dog and collected the lymph. They then isolated a loop of small intestine and injected into it toxic material from the intestinal content of a dog that had died from obstruction. This done, they increased the pressure within the closed loop by means of a column of water. They noticed that the lymph soon became bloody. The material, when injected, caused toxemia and death with the typical picture. Normal lymph, they found, was not toxic.

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136. Dragstedt; Dragstedt, and Chase (footnote 86). McClintock; Dragstedt, and Dragstedt (footnote 21).

137. Stone; Bernheim, and Whipple (footnote 7). Whipple and Cooke (footnote 34). Whipple, G. H.; Stone, H. B., and Bernheim, B. M.: Intestinal Obstruction: A Study of a Toxic Substance Produced in Closed Duodenal Loops, *J. Exper. Med.* 17:286, 1913.

138. Dragstedt; Dragstedt; McClintock, and Chase (footnote 15, first reference).

139. McLean, A., and Andries, R. C.: Ileus Considered Experimentally, *J. A. M. A.* 59:1614 (Nov. 2) 1912.

140. Sauerbruch, F., and Heyde, M.: Weitere Mittheilungen über die Parabiose bei Warmblütern mit Versuchen über Ileus und Urämie. *Ztschr. f. exper. Path. u. Therap.* 6:33, 1909.

lowing question arises: Is this toxin the cause of the toxemia? Does it actually find its way into the circulation? If so, how?

*Question 26.*—Is this toxin the cause of the toxemia?

This question can best be answered by comparing the syndrome of injection with that of obstruction. In this, it seems best to compare strangulation with injection because in strangulation the toxemia is developed to the greatest extent. This data is given in the accompanying table.

*Comparison of the Syndrome of Injection with Strangulation*

	Strangulation	Injection
	Clinical	
Vomiting .....	+	+
Tenesmus .....	—	+
Diarrhea .....	—	+
Dilatation of pupil.....	No observation	+
Tremor, weakness in hind legs.....	+	+
Weak, rapid pulse.....	+	+
Low blood pressure.....	+	+
Death in coma.....	+	+
	Blood	
Leukopenia .....	+	No observation
Fibrin increased .....	+	No observation
Loss of coagulability.....	No observation	+
High urea .....	+	+
	Urine	
Amount .....	Scanty	Increased
Trace of albumin.....	+	+
High nonprotein nitrogen.....	+	+
Kidney function approximately normal.....	+	+
	Pathology	
Central nervous system normal.....	+	+
Lungs normal .....	+	+
Liver .....	Normal	Engorged
Spleen .....	Normal	Engorged
Pancreas .....	Normal	Engorged
Splanchnic dilatation .....	+	+
Stomach distended .....	+	—
Intestine distended .....	Above obstruction	—
Large amount of fluid in intestine.....	+	+
Intestinal mucosa injected.....	+	+

These comparisons have been found in different parts of the literature and it does not seem necessary to quote all the references. Whipple and his co-workers<sup>135</sup> go into this comparison more deeply than do any of the other authors. There truly is a marked resemblance. Possibly the differences can be explained by the fact that in one case there is mechanical obstruction and slower absorption, whereas in the other an overwhelming dose is given all at once.

Whether or not they resemble each other enough to be considered due to the same process is largely a matter of personal opinion.

135. Stone; Bernheim, and Whipple (footnote 7). Whipple and Cooke (footnote 34).

Enderlen and Hotz <sup>141</sup> studied the absorption of sodium chloride and dextrose in 5 per cent solutions. They found that normally the substances were absorbed in quantities proportional to the fluid absorbed. In simple obstruction, they found the absorption much decreased and much excess of fluid secreted into the lumen. They also found absorption much decreased in closed loops.

Davis <sup>44</sup> found phenolsulphonphthalein actively absorbed by closed loops as tested by its excretion in the urine.

Falloise <sup>45</sup> injected the toxin into the lumen of gut, the mucosa of which had been damaged by sodium fluoride or hot water. He noted toxic symptoms.

Hartwell and his co-workers <sup>142</sup> were the first to bring out the theory that the toxemia did not make its appearance in the presence of uninjured mucosa. They recognized the great difference between simple obstruction and strangulation and attributed it to this. They searched all the protocols of Whipple and his co-workers and found that in every case in which death supervened with obstruction or closed loop, there were gross changes in the mucosa. They even carried it so far as to state that when obstruction or closed loop was caused by section and inversion, the element of injury to the mucosa was automatically introduced by the surgical procedure. They then devised a clamp with which to cause obstruction without compromising the circulation of the compressed gut. They claimed that dogs thus obstructed died only from starvation provided their water balance was maintained. They later modified this view and decided that damage done by section was immaterial.

Brooks and his co-workers <sup>143</sup> believed absorption through the injured mucosa was the most important factor in the production of the toxemia. They agreed with Hartwell that the toxemia is directly proportional to injury to the mucosa. They believed that this injury is caused largely by distention of the gut and the resultant compromising of the circulation. They called attention to the fact that the upper intestine is largely secretory in function, while the lower is largely absorptive. Thus in upper intestinal obstruction, the distention and resultant damage to mucosa makes its appearance much more rapidly than in lower intestinal obstruction. In this way they explained the extreme toxicity of strangulation and the fact that long closed loops are less rapidly fatal than short ones in which distention appears more

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141. Enderlen and Hotz: Ueber die Resorption bei Ileus und Peritonitis, Mitt. a. d. Grenzgeb. der Med. u. Chir. 23:755, 1911.

142. Hartwell (footnote 27, first reference). Hartwell and Hoguet (footnotes 17 and 72). Hartwell; Hoguet, and Beckman (footnote 11).

143. Brooks; Schumacher and Wattenburg (footnote 20). Copher and Brooks (footnote 23). Murphy and Vincent (footnote 29).

Sauerbruch and Heyde<sup>140</sup> experimented with animals living in parabiosis. They found that when one was obstructed they both showed symptoms. If they were then separated, the one that was not obstructed recovered.

Sugito<sup>6</sup> produced closed loops in dogs. During the last moments of life, he aspirated blood from the veins in the mesentery coming from the loop. He then separated the serum from this blood and injected it into mice. He found that it killed them in from three to fourteen hours. He found that serum from the mesenteric veins of normal animals was nontoxic. Scholefield<sup>32</sup> corroborated these observations of Sugito and emphasized the fact that the blood must be obtained during the last moments of life to show toxicity.

Sugito<sup>6</sup> claimed that the toxin could be isolated from the blood of animals with obstruction by tryptic digestion of serum albumin.

Schloss<sup>99</sup> reported a histamine-like body which he recovered from the blood of infants suffering from obstruction.

There is then some evidence of a toxin circulating in the blood. If the toxin does get into the blood, what possible channels of entrance are there?

*Question 28.*—Does toxin get in through the intestinal mucosa?

It has been amply proved that the normal intestinal mucosa is impervious to the toxin (fact 10), but the mucosa above an obstruction cannot be called normal. It nearly always shows gross changes, and there is no reason to believe that, even in the absence of any gross or histologic changes, its physiology is not profoundly affected. In studying the absorptive properties of the intestine above an obstruction, the presence of indican and phenol in the urine (Kukula<sup>46</sup>) may be taken as evidence of absorption from the obstructed gut.

Braun and Boruttau<sup>49</sup> injected strychnine into the lumen of normal gut in quantities varying from 1.2 to 3 mg. Cramps began in five and one-half minutes, and death in thirteen and one-half minutes. In animals with obstruction which received like doses they observed the onset of cramps in between ten and fifteen minutes and death supervened in from twelve and one-half to thirty-five minutes. They took this as proof of the fact that absorption was present but lessened in obstructed gut.

Clairmont and Ranzi<sup>39</sup> injected calcium iodide (205 cc. of a 2 per cent solution) into the lumen of the gut and then tested the urine at frequent intervals for the presence of iodine. In this way they constructed curves for normal and obstructed animals which they took to be indices of the absorption of this element. After many experiments they determined that the absorption above an obstruction was more than normal at first, reaching a peak at about the end of the first half of the survival period. After that it rapidly fell below normal.

The probability of the toxins being absorbed is accepted by the great majority of investigators. There is good proof that such is the case. On the other hand, it is difficult to imagine how toxin can be absorbed through the vascular elements of the mesentery in cases of strangulation in which at least the venous return is cut off and often the entire circulation is blocked. It should again be emphasized that death can occur in strangulation without peritoneal infection.

*Question 29.*—Is, then, the toxin absorbed by the peritoneum after passage through the intestinal wall?

The work of Stone and Firor<sup>144</sup> already described, in which they demonstrated toxicity of Ringer's solution which had contained an inflated closed loop of intestine filled with toxin would suggest this.

Braeye<sup>147</sup> held the theory that the intestinal wall was in some respects similar to a semipermeable membrane and would therefore conform to the laws of diffusion and osmosis. He quoted recent work which showed that a collodion membrane, impermeable to hemoglobin, could be made permeable by adding sodium oleinate and sodium glycocholate to the mixture. He therefore put an excised closed loop, full of toxin, into Ringer's solution and added 1 per cent soap solution. He was not able to demonstrate toxicity of the Ringer's solution.

Foster and Hausler,<sup>26</sup> working on this theory, put a strangulated loop in a rubber bag in an attempt to eliminate peritoneal absorption. They were not able to demonstrate any difference in the outcome.

The work of Schönbauer<sup>33</sup> deserves special consideration. He observed that a strangulated inguinal hernia was not nearly as fatal as a strangulated internal hernia. He ascribed this to the surroundings of the strangulated loop. He carried out the following experiments along this line:

Schönbauer put calcium iodide in the stomachs of normal animals by means of a stomach tube. He was unable to demonstrate any signs of absorption over a period of twelve hours as indicated by frequent examinations of the blood and urine, nor was he able to demonstrate any evidence of the substance in the peritoneal cavities of these animals.

He next repeated these experiments, except that after placing the calcium iodide in the stomach, he subjected the animal to a normal exploratory laparotomy. After this procedure, he found traces of the substance in the blood in six hours and large amounts in the peritoneal cavity at subsequent postmortem examination.

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147. Braeye, L.: Contribution to the Study of Toxic Absorption from the Intestinal Tract in Experimental High Obstruction, *Bull. Johns Hopkins Hosp.* 40:33, 1927.

rapidly due to their very shortness. They feel that they proved the permeability of injured mucosa to the toxin by their experiment with a cannula in the thoracic duct which has already been described. They connect this theory with their theory of the bacterial origin of the toxin and state that there are two factors in the production of the toxemia of obstruction: (1) the elaboration of the toxin, which is the result of bacterial action, and (2) the absorption of the toxin which is proportional to injury to the mucosa. Of these two factors, they feel absorption to be by far the most important. In this way they feel that they have explained how the toxin can be of bacterial origin and still cause death more rapidly in obstruction in the upper reaches of the intestinal tract.

Stone and Firor<sup>144</sup> felt that high intra-intestinal pressure was the cause of the absorption of the toxic substance. They found that the normal intra-intestinal pressure was 1.5 cm. of water whereas the pressure above obstruction was over 150 cm. of water. They then tested the absorption of india ink from the normal intestine and found there was none. However, when they placed the substance in the lumen of the gut above an obstruction, they recovered it from the mesenteric glands and lymphatics. They then excised a loop of normal intestine, filled it with the toxic substance and placed it in Ringer's solution. They found that if they then inflated the loop with air, the Ringer's solution rapidly became toxic as tested by injection into an animal. This experiment does not, however, rule out damage to the mucosa.

This theory of absorption, as stated most clearly by Brooks and his co-workers, is held by many other investigators (Scholefield,<sup>32</sup> Gatch, Trusler and Ayers,<sup>25</sup> Wilkie,<sup>19</sup> Dragstedt, Dragstedt and co-workers,<sup>145</sup> Foster and Hausler,<sup>71</sup> Eisberg<sup>5</sup> and others). Van Beuren<sup>146</sup> found that in experimental simple obstruction the lesions of the mucosa usually first appeared at the end of forty-eight hours. He suggested that the toxemia begins at this time, and compares it with the well known clinical fact that in cases of obstruction surgical intervention is of little aid after the obstruction has persisted for over forty-eight hours.

I find but few opinions which oppose the theory that toxic absorption occurs through injured mucosa. The outstanding one is that of Whipple and his co-workers, whose theory has already been discussed in detail.

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144. Stone, H. B., and Firor, W. M.: Absorption in Intestinal Obstruction: Intraintestinal Pressure as a Factor, *Tr. South. Surg. & Gynec. Ass.* **37**:173, 1924.

145. Dragstedt; Dragstedt; McClintock, and Chase (footnote 15). Dragstedt; Moorhead, and Burky (footnote 41, second reference). McClintock; Dragstedt and Dragstedt (footnote 21).

146. Van Beuren, F. T., Jr.: Relation Between Intestinal Damage and Delayed Operation in Acute Mechanical Ileus, *Ann. Surg.* **72**:610, 1920.

it is elaborated in the intestine or mucosa, and finds its way, by one or more of a number of devious passages, to the circulation. By means of the circulation, it is carried to the various parts of the body, bringing with it destruction and death.

*Question 31.*—Does the toxin act on the central nervous system?

There is nothing in the pathologic picture which points to any actual destruction of nervous tissue; however, some observers have remarked concerning certain nervous manifestations.

Clairmont and Ranzi<sup>89</sup> observed symptoms mostly of a nervous character. They added brain substance to the toxin before injection and claimed to demonstrate a lessened toxicity. They further injected brain extract from a dog which had died from obstruction, and found that it killed a mouse in two days.

Magnus-Alsleben<sup>104</sup> isolated a substance from the upper intestinal tract of dogs. When this substance was injected into rabbits in small amounts, it caused general central paralysis, cramps and death due to respiratory stoppage.

Fallose<sup>46</sup> injected extract of feces and obtained a fall in blood pressure, dyspnea, clonic and tonic convulsions, exophthalmia and dilatation of the pupils.

Nesbitt<sup>112</sup> thought the toxic substance was choline, which is a powerful nerve poison.

Sugito<sup>6</sup> reported that he isolated the toxin from the brain of animals dying from obstruction. This substance, he states, is especially plentiful in the medulla.

*Question 32.*—Does the toxin act on the heart and large vessels?

There is no evidence of any action of the toxin on the heart and large vessels.

*Question 33.*—Does the toxin act on the lungs?

There is no evidence of any action of the toxin on the lungs

*Question 34.*—Does the toxin act on the liver?

The liver has received attention because, if the toxin is absorbed through the portal system it is the first organ to be affected.

Hartwell and Hoguet<sup>17</sup> described fatty changes in the liver at post-mortem examination and compared them to those found in the toxemias of starvation, pregnancy, delayed chloroform poisoning and acute infections. Draper<sup>10</sup> and others could not find such changes.

Colp and Louria<sup>149</sup> emphasized the fact that increased blood urea is not seen in liver insufficiency. They were unable to find any marked changes in liver function as demonstrated by the phenoltetrachlorophthalein test.

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149. Colp, R., and Louria, H. W.: Liver Function in Intestinal Obstruction, *Arch. Surg.* 10:756 (March) 1925.

He made the following experiment to test whether the blood or the peritoneum received the substance first: After placing the calcium iodide in the stomach, he performed a laparotomy and washed the peritoneal cavity out with silver acetate, leaving some free in the abdomen at closure. In six hours, the dogs were very ill. He was unable to find any calcium iodide in the blood or urine, but on opening the peritoneal cavity he found a large precipitation of silver iodide and free calcium iodide.

He obtained the same results when similar methods were applied to simple obstruction and strangulation. Then he tested in a similar way the diffusion of various other substances through the intestinal wall. He found that crystalloids passed through more rapidly than colloids, and that bacteria did not pass through.

His experimentation is a great argument in favor of the most careful handling of intestines at operation.

Thus evidence shows that it is possible for substances to pass through the wall of compromised gut and be absorbed by normal peritoneum.

All the avenues of absorption having been considered, there is one remaining possibility by means of which the toxin can reach the circulation.

*Question 30.*—Is the toxin rather formed by the cells of the mucosa and secreted in both directions (i.e., into the intestinal lumen and into the blood stream)?

Many of the end-products of digestion are actually passed through the cells of the intestinal mucosa and these same cells secrete certain substances into the intestinal lumen. This theory is not so improbable as may at first seem. It is further attractive to the imagination because a similar phenomenon occurs in acute pancreatitis.

Whipple and his co-workers<sup>148</sup> were the chief advocates of this theory. It does not seem necessary again to describe their work.

Ellis<sup>36</sup> was also attracted by this theory, although he admitted the difficulty of proof. He made the suggestion that the bacteria may activate the mucosa cells to form the toxin.

Davis<sup>44</sup> at one time was inclined to favor this theory. He thought the normal contents were toxic in the upper intestine where there are no bacteria, and that a perverted action of the mucosa would cause the injection of this substance into the blood stream. He arrived at this rather by the process of elimination.

The subject of the toxin has been discussed from all possible angles. It seems as if the majority of the evidence would point to the fact that

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148. Stone; Bernheim, and Whipple (footnote 105, first reference; footnote 42; *Intestinal Obstruction: IV. Mechanism of Absorption from Mucosa of Closed Duodenal Loops*, J. Exper. Med. 19:166, 1914). Whipple (footnote 50, first reference).



- (2) Bloody exudate in the lumen of the gut.
- (3) Congestion of the pancreas.

From the blood chemistry they note the following :

- (1) Marked rise in the urea.
- (2) Slight fall in the chlorides.

Sweet and Pemberton<sup>120</sup> noted an inhibitory action of suprarenal extract on pancreatic secretion regardless of changes in blood pressure.

Sweet<sup>116</sup> suggests epinephrine as a treatment for the toxemia of obstruction.

Of what significance is this similarity?

Another interesting and similar condition is anaphylaxis.

*Question 39.*—Is the toxemia in any way similar to an anaphylactic phenomenon?

This subject has already been mentioned in relation to the closely allied condition, protein intoxication.

A number of workers have remarked on the close similarity of toxic injection and anaphylactic shock in dogs (Whipple and his co-workers,<sup>153</sup> Sweet,<sup>38</sup> South and Hardt<sup>13</sup>).

Louria<sup>154</sup> described urticaria in a case of high obstruction.

Rackemann, Longcope and Peters<sup>76</sup> described low amounts of blood chlorides in serum sickness.

The following description of the picture of anaphylaxis in dogs is found in the combined works of Hisanobu,<sup>155</sup> Major,<sup>156</sup> Webb,<sup>157</sup> and Weil.<sup>64</sup>

#### Symptoms :

- (1) Vomiting.
- (2) Staggering gait, weakness in hind legs.
- (3) Collapse, tremor.
- (4) Low blood pressure.
- (5) Weak, rapid pulse.

#### Pathology :

- (1) Intense congestion and hemorrhage of the gastro-intestinal tract.
- (2) Lungs, pleura and endocardium congested.
- (3) Congestion of liver.

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153. Stone; Bernheim, and Whipple (footnote 7). Whipple; Rodenbaugh, and Kilgore (footnote 90, third reference).

154. Louria, H. W.: The Blood Urea Nitrogen in Acute Intestinal Obstruction, *Arch. Int. Med.* 27:620 (May) 1921.

155. Hisanobu, K.: On the Distribution of the Non-Protein Nitrogen in Cases of Anaphylaxis and Peptone Poisoning, *Am. J. Physiol.* 50:357, 1919.

156. Major, R. H.: Blood Chemistry in Allergy, *Bull. Johns Hopkins Hosp.* 34:104, 1923.

157. Webb: The Mechanism of Anaphylactic Leucopenia in Dogs, *J. Path. & Bacteriol.* 27:79, 1924.

Draper and Schultz<sup>150</sup> quoted Pohl in affirming that conjugation of camphor and glycuronic acid takes place in the liver. They thought that they demonstrated a slight reduction of liver function by this test.

*Question 35.*—Does the toxin act on the other splanchnic organs?

There is evidence of marked effect on the splanchnic organs, as shown by vomiting, bloody diarrhea, tenesmus, splanchnic congestion, engorgement of the liver, spleen and pancreas, and injection and ulceration of the intestinal mucosa. Whether this is due to direct or reflex action is not clear.

*Question 36.*—Does the toxin act on the kidneys?

There are signs of slight renal damage as evidenced by albuminuria, occasional casts, slightly reduced ability to excrete urea and sodium chloride.<sup>60</sup> This has already been discussed in detail.

*Question 37.*—Does the toxin act on all the cells of the body?

There is good evidence that the toxin produces rapid breakdown of protein molecules. This is indicated by the extreme and rapid rise in the urea in both blood and urine. This, too, has been discussed in detail.

*Question 38.*—Does the toxin act on the glands of internal secretion?

There is a certain strange and peculiar similarity between dogs that have died from toxic injection and those which have died after bilateral suprarenalectomy.

This was first noticed by Sweet<sup>151</sup> and Ellis.<sup>30</sup> They found that dogs died after bilateral suprarenalectomy with a picture indistinguishable from that following toxic injection. What is more, they were able to recover a similar toxin from the intestinal tracts of dogs dying from the former condition.

Stewart and Rogoff<sup>152</sup> described the following striking symptoms observed in suprarenalectomized dogs:

- (1) Vomiting.
- (2) Bloody diarrhea.
- (3) Tremors, weakness and convulsions.
- (4) Temperature normal or subnormal.

At postmortem examination, Stewart and Rogoff described the following observations:

- (1) Deep injection and frequent ulceration of the entire gastro-intestinal tract, most in the duodenum.

150. Draper, J. W., and Schlutz, F. W.: Glycuronic Acid Determination (Tollens) in Duodenal Obstruction, *Proc. Soc. Exper. Biol. & Med.* 9:28, 1911-1912.

151. Sweet (footnote 117, first reference).

152. Stewart and Rogoff (footnote 63); Studies on Adrenal Insufficiency in Dogs: I. Control Animals not Subjected to Any Treatment, *Am. J. Physiol.* 78: 683, 1926.

The great objection to the theory of shock is the meager experimental proof. There cannot be any question about the fact that the picture of high obstruction, whereas it may simulate shock in some respects, is widely different in others. Shock may be an element in some cases, but it cannot possibly explain the whole phenomenon.

Another group of workers claims that death is due to disturbance in the acid-base mechanism and dehydration plus starvation. This has been fully discussed elsewhere. In view of what has been brought out heretofore, it seems evident that they are only dealing with part of the picture. They confine all their work to simple obstruction and do not attempt to explain closed loops or strangulation. Their explanation does not seem to be entirely adequate even for simple obstruction, because toxic symptoms do occur here.

Draper Maury<sup>118</sup> suggested that death may be due to the loss of some internal secretion which is elaborated by the duodenum and small intestine and is essential to life. This is definitely refuted by the fact that dogs will live indefinitely with the entire duodenum removed and have been kept alive three months after the removal of the pylorus, duodenum and upper part of the jejunum.

Ellis<sup>30</sup> said the fact that an identical poison is recovered from the gastro-intestinal tract after toxic injection suggests some physiologic dysfunction.

It seems appropriate, under this heading, to discuss the work of Werelius.<sup>80</sup> He studied drained duodenal loops and noticed that in twenty-four hours the secretion of bile stopped, and the bile was replaced by a clear mucoid or reddish fluid. This change in the character of the biliary secretion predicted serious symptoms and death. He used this as the basis of his theory, in which he claimed that the liver depended for its normal function on the nervous reflexes derived from normal peristalsis. Therefore, if the intestine became aperistaltic for one reason or another, the liver ceased to function, and death resulted from this insufficiency. He applied this to intestinal obstruction, claiming that the intestine below an obstruction became aperistaltic and thus reflected on liver function. In this way he attempted to explain why high obstruction was more fatal than low, i.e., because it resulted in more aperistaltic gut. He claimed that the high amount of urea was not an argument against liver insufficiency, because urea could be formed in other organs as well. This is an original idea, but lacking in experimental proof. It is further weakened by the symptomatology he described in his animals: (1) subnormal temperature, (2) albuminuria, (3) leukocytosis 20,000, (4) low blood sugar, (5) increased urea and (6) low carbon dioxide.

Blood:

- (1) Leukopenia.
- (2) High nonprotein nitrogen, chiefly due to urea.
- (3) Rise in creatinine.
- (4) Fall in chlorides.

Flashman<sup>158</sup> reported that bilateral suprarenalectomy in rats increases their susceptibility to anaphylactic shock.

This provides more food for thought.

*Question 40.*—Finally, is there no toxemia and is death rather physiologic in character, being due to lack of some substance or substances necessary for life, or to nervous shock?

The theory of shock or a shock-like condition has attracted a few observers as a possible cause of death in strangulation.

Braun and Boruttau<sup>49</sup> expressed the opinion that the nervous impulse due to occlusion not only has a mechanical action on peristalsis, but increases secretion to a great extent. This, they think, leads to such a diminution of circulatory fluid that the animal dies of inanition, comparable to death by exsanguination. They took kymographic records of animals dying in both conditions and found a great similarity.

McLean and Andries<sup>159</sup> propounded a somewhat similar theory. Being unable to demonstrate any toxic material, they felt that death was due to a depletion of the vascular and lymph systems causing grave disturbance of circulation, especially cerebral. They thought that a loss of sympathetic control played a large part in this phenomenon.

Foster and Hausler<sup>159</sup> felt that shock plays a large part in strangulation. They thought that a long loop is more rapidly fatal than a short one. They used this in building up their theory, saying that the shock is due to pain, glandular inactivity and loss of blood into the strangulated bowel. They felt that toxic absorption is practically a negligible factor, emphasizing the fact that nothing can be absorbed from a strangulated loop due to interference with the circulation. They thought that they had eliminated peritoneal absorption; then death resulted from a strangulated loop that had been placed in a rubber bag. Van Beuren,<sup>160</sup> von Khantz<sup>161</sup> and Wilkie<sup>51</sup> also thought that shock plays an important rôle.

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158. Flashman, D. H.: Effect of Suprarenalectomy on Active Anaphylactic Shock in the White Rat, *J. Infect. Dis.* 38:461, 1926.

159. Gamble; Blackfan, and Hamilton (footnote 8, first reference). Foster and Hausler (footnote 82, second reference).

160. Van Beuren, F. T., Jr.: Lethal Factors in Acute Ileus, *Ann. Surg.* 75: 423, 1922.

161. von Khantz, A.: Zur Frage der Bakteriämie bei Ileus und postoperativer Darm lähmung, *Arch. f. klin. Chir.* 88:412, 1908-1909.

# URETERAL ACTIVITY IN SOME PATHOLOGIC CONDITIONS

STUDIED BY THE GRAPHIC MANOMETRIC METHOD \*

HARRY ROBERT TRATTNER, M.D.

CLEVELAND

In 1924, I published some observations on peristalsis of the intact human ureter obtained by means of a graphic method. Since that time additional physiologic data have been gathered and records taken in a number of pathologic cases.

The object of this work is to throw greatly needed light on the hitherto meager knowledge of the behavior of the human ureter, and to give to the urologist a method that admits of easy application in the clinic, so that it is possible to recognize disturbances of ureteral function.

In a review of the literature it was found that studies devoted to the physiology and physiologic pathology of the human renal pelvis and ureter are comparatively few. More numerous, however, are the investigations which have been conducted on animal ureters, intact and excised.

## METHODS OF STUDY

The methods of study of ureteral activity may be classified as follows: (1) ocular observations—direct and indirect; (2) electro-ureterographic, and (3) graphic.

*Ocular.*—Direct ocular observations are made by exposing a section or the entire extent of the ureter, leaving it in situ, or excising and placing the organ in a bath of oxygenated Ringer's or Locke's solution. Investigations made simply by watching the ureteral waves are obviously inexact, particularly on the intact organ, because of the confusion of ureteral movements with those of the neighboring organs as well as the inability of the eye to follow many of the waves which are either too small or too rapid to be seen. For example, while one follows the wave from the renal pelvis, where it is usually initiated, to the bladder, one or more contractions may have followed the preceding one so closely that when the eyes are again directed to the renal pelvis, these con-

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\* From the Department of Urology, Cleveland City Hospital, and the Department of Pharmacology, Western Reserve University.

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## SUMMARY

Certain facts stand out and should be emphasized.

1. In high obstruction two different processes are involved: (a) a profound disturbance in the acid-base mechanism resulting in alkalosis and dehydration and (b) a definite toxemia. In simple obstruction, the first process is the more prominent and often fills the whole picture. However, toxemia may enter also to a varying extent. On the other hand, in closed loops and strangulation, the toxemia is on the ascendency and often crowds everything else out.

2. There is a toxin in the lumen of the obstructed gut and it looks very much as if it reached the blood stream and was responsible for the toxemia. The origin of this is not clear. Those who say that it is formed by bacteria must prove:

- (a) Why high is more fatal than low obstruction.
- (b) Why the toxin appears so rapidly after obstruction.
- (c) Why the toxin appears in the gut immediately after toxic injection.

(d) Why the toxin appears in such conditions as clotting of the portal vein, acute pancreatitis, and bilateral suprarenalectomy, when there is no obstruction.

Those who claim that it is not formed by bacteria must prove its formation in their absence.

3. There seems to be some mysterious connection between the toxemia of high obstruction, acute pancreatitis, bilateral suprarenalectomy and anaphylaxis.

I shall not attempt to draw conclusions myself. I should, however, like to emphasize the fact that more work should be done on strangulation. In this condition, toxemia is developed to its highest degree. The alkalosis and dehydration can be controlled. However, one rarely sees cases of simple obstruction in the clinics without the complication of toxemia; therefore, there remains the necessity of finding a means of combating this dread condition.

What is the cause of death in high obstruction?

2. A cannula is inserted into the ureter, the cannula being attached to a water manometer and this to a piston recorder. Lucas and Satani employed this method, but no description is given of the manner in which the urine was prevented from accumulating.

3. Muscle levers are attached to the ureteral wall. This method records the activity of the longitudinal muscular coat. Obviously it cannot be used on the intact unexposed ureter.

4. The New Graphic Method: The chief objection to the work on the intact organ has been the lack of an adequate method. This difficulty has, I think, been overcome in the apparatus herein described, because (a) ureteral activity is recorded while permitting a practically unobstructed urinary escape; (b) the method is adaptable to the intact unexposed human ureter as well as to the exposed or excised animal ureter, and (c) the method is of minimum inconvenience to both patient and operator.

The manometer, although the same as the earlier model in principle, has been improved so that it is more sensitive and easier of manipulation. In order to establish the degree of peripheral resistance at which contractions are most satisfactorily maintained and to simulate intravesical pressures, a finely threaded screw adjustment is now employed, thus permitting a regulation of the outflow to any desirable extent (fig. 1). By means of this instrument, graphic records have been taken from man, and from the dog and rabbit. Consecutive tracings have been taken for as long as ten hours from the intact and excised ureter of the dog. In the human studies, a comparison of the activity of the ureter of one side is usually made with that of the other by using one manometer alternately. The upper, middle and lower portion of the ureter may be examined separately by placing the end of the catheter at the desired level. Simultaneous records of the activity of both ureters have been made by employing two manometers. In a case of bilateral complete ureteral duplication, a simultaneous tracing was taken from all four ureters with four manometers.

By this method the activity of the circular muscle of the ureter is recorded, but since the longitudinal and circular muscles (the latter being composed of more muscle fibers, and therefore the stronger of the two coats) usually contract simultaneously, the record obtained is a fair representation of ureteral activity.

In my first paper it was pointed out that the ureter seems to possess two chief types of waves, namely, the small more rapid pendulum movements that are not concerned with the propulsion of urine, and the slower more powerful peristaltic contractions that are usually accompanied by an outflow of urine. The rate and amplitude of these types

tractions have passed unnoticed. If only one point on the ureter is observed, it is difficult to differentiate between local contractions and those that pass the entire length of the ureter.

Indirect ocular observations have been made by watching the activity of the lowermost section of the ureter through the cystoscope. Data obtained in this manner are not wholly reliable because there may be inactivity of the upper and middle portion, while the lower section of the same ureter may be functionally competent.

Studies of ureteral activity have also been conducted with the aid of the fluoroscope either during or after the injections of opaque solution. This method is open to the following objections:

1. The view is not sufficiently clear because of diffusion by intervening tissue and organs.

2. Only short observations are possible because of the danger of overexposure to the roentgen ray.

3. The intra-ureteral injection of any fluid toward the renal pelvis gives rise to abnormal activity of various degrees depending on the pressure of injection, the position of the catheter in the ureter, the amount, kind and strength of solution employed.

Thus the emptying time of the renal pelvis could be hastened or delayed through a physiologic disturbance of the nature of hyperactivity, spasticity or temporary abolition of peristalsis.

*Electro-Ureterographic.*—In 1914, Orbeli and Brucke obtained electro-ureterograms in the rabbit by placing two electrodes a short distance apart on the outer wall of the ureter and attaching them to a galvanometer. They found that the smooth muscle of the ureter in situ, delivers rhythmic current variations of the triphasic ground type. I have attempted to obtain an electro-ureterogram from the intact human ureter by placing one electrode in the ureteral lumen and the other on the skin in the region of the renal pelvis, the electrodes being connected to the electrocardiograph. The result was that cardiac contractions were found superimposed on other current variations which probably represent ureteral current phenomena. Thus far this method has not been found applicable to the intact unexposed ureter.

*Graphic.*—Records of ureteral peristalsis have been obtained in animals by graphic methods as follows:

1. A rubber capsule is bound to one end of a catheter which is inserted into the ureter and the capsule ballooned out, the free end of the catheter being connected with an ordinary recording tambour. Fagge first recorded contractions from the intact animal ureter by this method. The objection to this procedure is that there is partial or complete obstruction to the flow of urine with the resultant effect of an increasing intra-ureteral pressure.



infiltration or thinning of the muscular coats through dilatation. The pain is usually more constant and dull rather than acute, but there may be acute exacerbations of pain. On vaginal examination, one or both ureters are found to be palpable and tender to pressure. The manometric tracing shows either a marked decrease in amplitude or total abolition of the peristaltic contractions. There is either a feeble

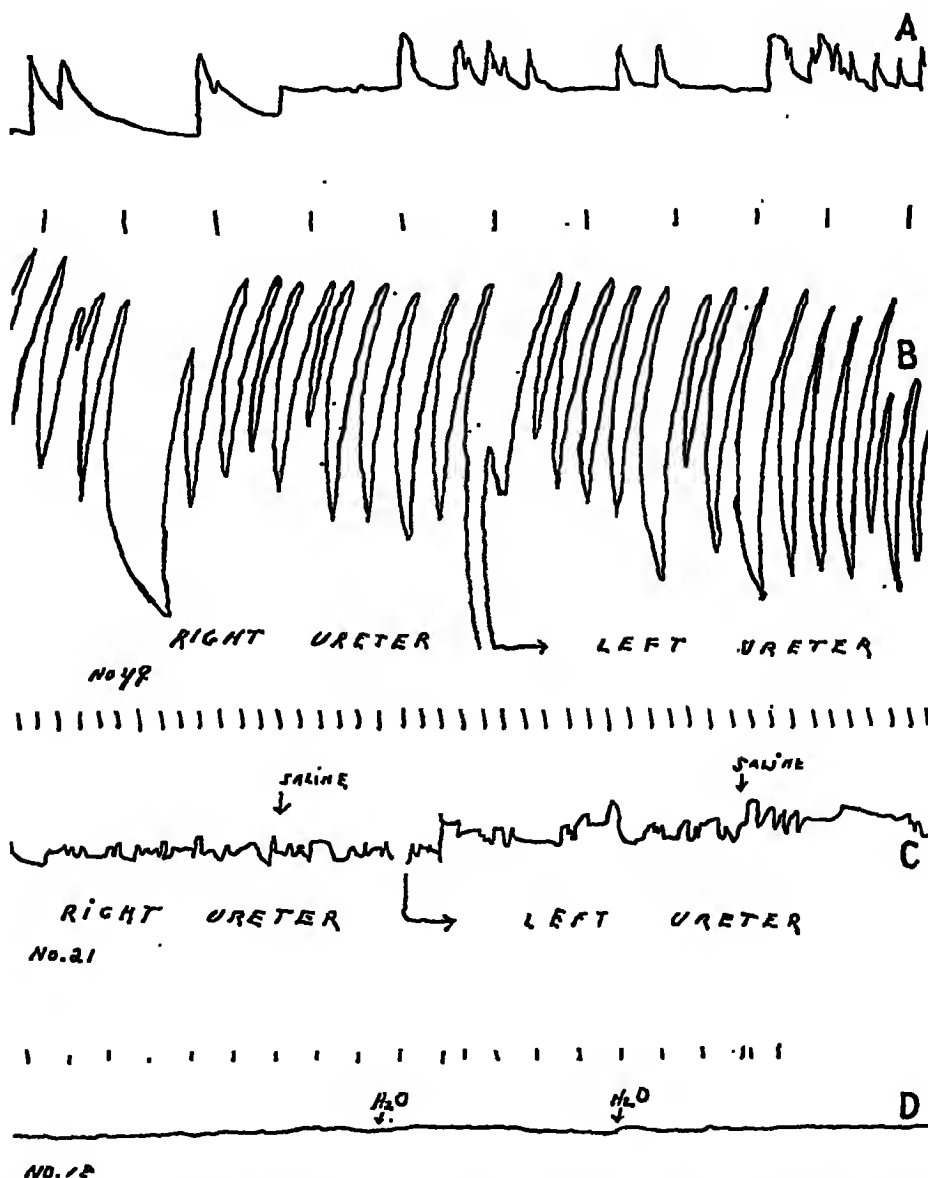


Fig. 3.—Typical tracings of the progressive degrees of ureteritis. *A* represents one type of a normal tracing; *B*, first degree ureteritis. There is an increase in the amplitude and rate of contractions (case 1). *C* is a tracing of second degree of ureteritis. There is a decrease in amplitude of contractions and there is little if any motor response to the intra-ureteral injection of saline. The ureters are hypotonic (case 4). *D* is a tracing of third degree ureteritis. There are no spontaneous contractions, and no motor response could be elicited by intra-ureteral injections of water. This demonstrates atonia or paralysis (case 26).

of waves vary, and they may be further subdivided into waves of various configurations. Ureteral tonus variations, tonic and spastic contractions may also be found. There may be a succession of various types of waves, they may be superimposed on each other, or the activity may be limited to one type only. Pressure on the ureter, changing the position of the patient (from recumbent to standing), moving the catheter, etc., usually alters rhythmical activity. Spontaneous alterations in rhythm may also occur.

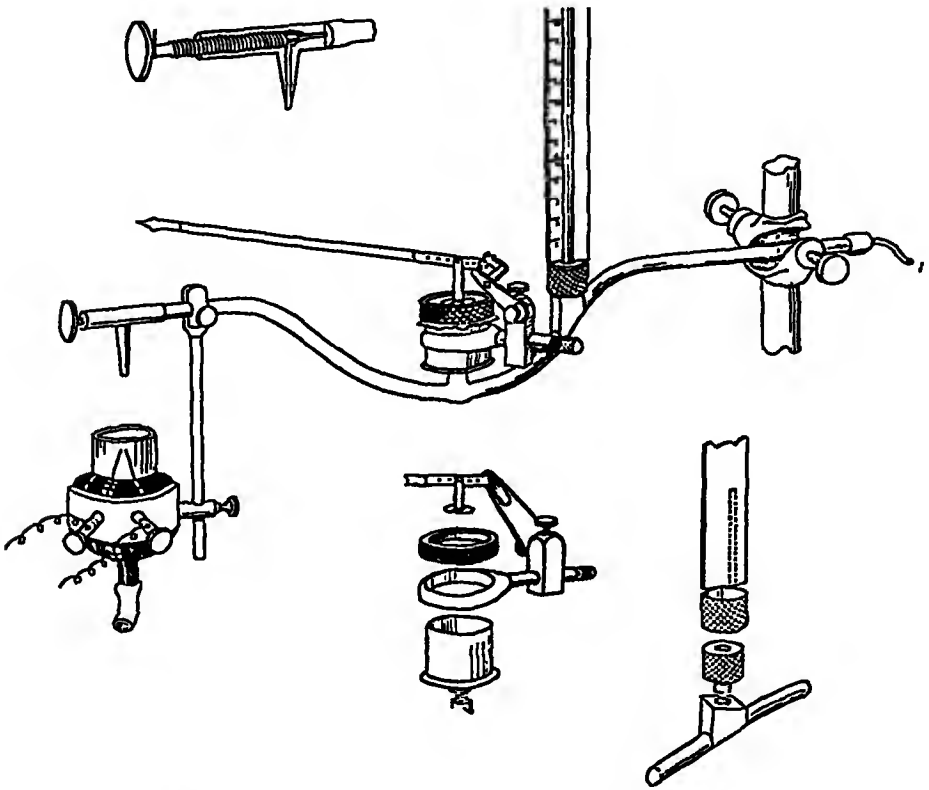


Fig. 1.—Diagrammatic drawing of the improved water manometer for the recording of ureteral peristalsis. The drop recorder is attached to the manometer (Biskind, M. S., and Dan, M.: *An Automatic Drop Recorder*, *Proc. Soc. Exper. Biol. & Med.* 26:52, 1928). Tambour cup, scale and lever mounting are removable. A longitudinal section of the outlet screw adjustment is shown.

Ureteral contractions may also be classified as (1) complete, i. e., those that pass the entire length of the ureter, (2) incomplete, i. e., those that arise in the renal pelvis but disappear before reaching the bladder, and (3) local, i. e., those which are confined to a small segment of the ureter. The manometer records the complete contractions and many of the incomplete ones, and when the latter immediately follow the former, the character of the waves is frequently bigeminal or trigeminal.

the back and thigh. There had also been nausea and vomiting. She was in the hospital three weeks before with the same complaint. Cesarean section had been done four months before.

On examination, tenderness was found in both lower abdominal quadrants and over the renal regions posteriorly; both ureters were palpable and tender vaginally. Cystoscopic examination showed a thick exudate coming from the right ureteral orifice. Infection was found only on the right side. Bilateral pyelo-ureterograms showed slight or moderate ureteral dilatation. Catheters were left in the ureters for twelve hours.

Manometric tracing showed atonicity of both ureters, there being no response to injections of water. A tracing repeated one week later, showed recovery of

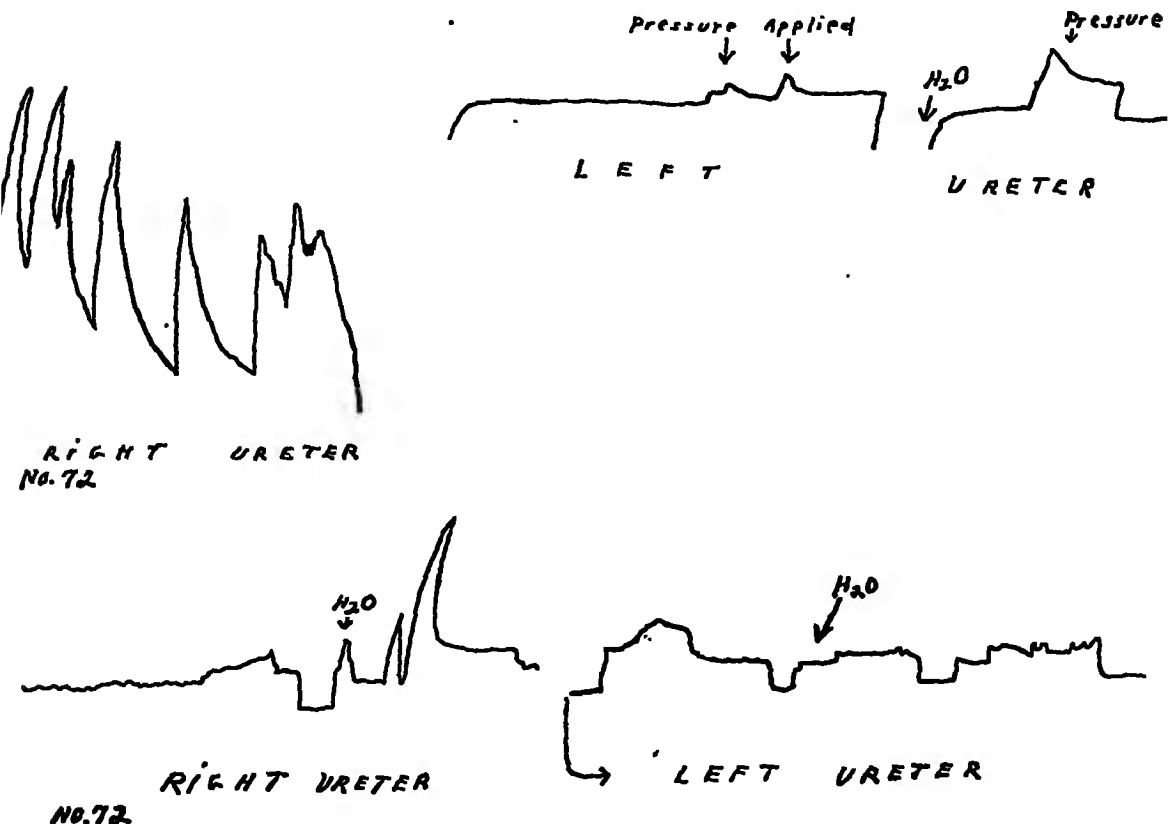


Fig. 5 (case 5).—The top tracing shows the left ureter to be atonic or paralyzed and the right ureter to possess a slight increase in activity. The lower tracing (taken six days later) shows hypotonicity of both ureters. There has been a progression from ureteritis of the first degree to that of the second degree on the right side.

activity of both ureters. At this time, the patient feels well and is free from symptoms (fig. 6).

CASE 7.—H. S., a woman, aged 31, had a condition clinically diagnosed ureteropyelitis of pregnancy (puerperal). She complained of backache and abdominal pain; she had had spontaneous normal delivery. A catheterized specimen of urine contained many white blood cells.

Cystoscopic examination showed a bilateral mixed infection (cocci and bacilli) with many white blood cells from each side. Pyelo-ureterograms showed bilateral

or no motor response to the intra-ureteral injection of fluid, which may return slowly or not at all through the catheter (even though the catheter fits the ureteral orifice snugly enough to prevent backflow of fluid along side it into the bladder). Ureters in this class may recover their activity, or there may be a progression of the process into that of permanent paralysis. The following cases are illustrative of this division:

**CASE 4.**—C. J., a woman, aged 28, complained of abdominal pain, dysuria and frequency of urination for the past four weeks. For the past two days, she had had chills and fever (104 F.). The patient had had a similar attack fourteen years before.

On examination, tenderness was found in the lower part of the abdomen. Both ureters were palpable and tender vaginally. Cystopic examination revealed a bilateral mixed infection (cocci and gram-negative bacilli). Bilateral pyelo-ureterograms appeared normal.

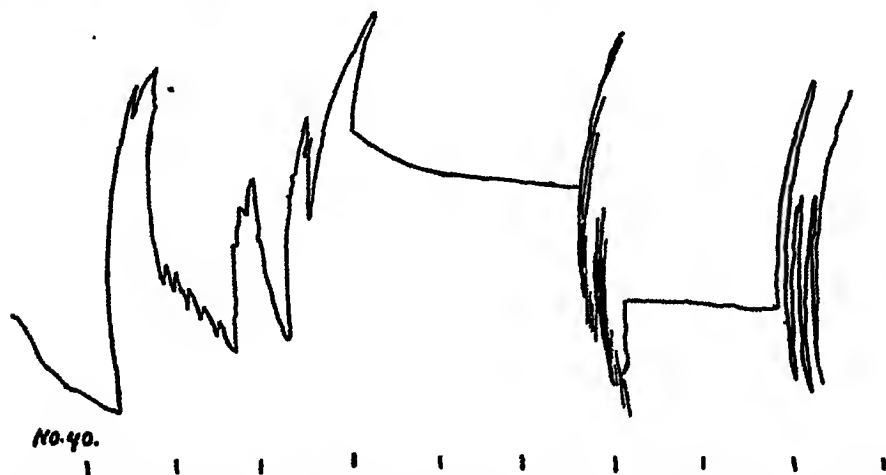


Fig. 4 (case 2).—First degree ureteritis. There is an increase in amplitude and an intermittent increase in the rate of contractions.

Manometric tracing showed hypotonus of both ureters (fig. 3 C).

**CASE 5.**—B. S., a woman, aged 20, had a condition clinically diagnosed pyelitis of pregnancy. Several hours after delivery, she had had a chill and complained of pain in the left lumbar region. For the past week there had been a dull pain radiating to the groin on this side.

On examination a week later, costovertebral tenderness was found on the left side; both ureters were thickened on vaginal examination. Cystoscopic examination showed right colon bacillus infection. Right pyelo-ureterogram showed a slight ureteral dilatation. Manometric tracing showed powerful peristaltic waves on the right side (ureteritis of first degree), atonic relaxed left ureter, there being no response to the injection of water; bimanual pressure of the left kidney was transmitted through the ureter. A tracing taken six days later showed that the right ureter was now also atonic. On this side, there had been a progression from ureteritis of the first degree to that of the second degree (fig. 5).

**CASE 6.**—A. B., had a condition clinically diagnosed subacute ureteropyelitis. She complained of pain in the right side of the abdomen radiating to

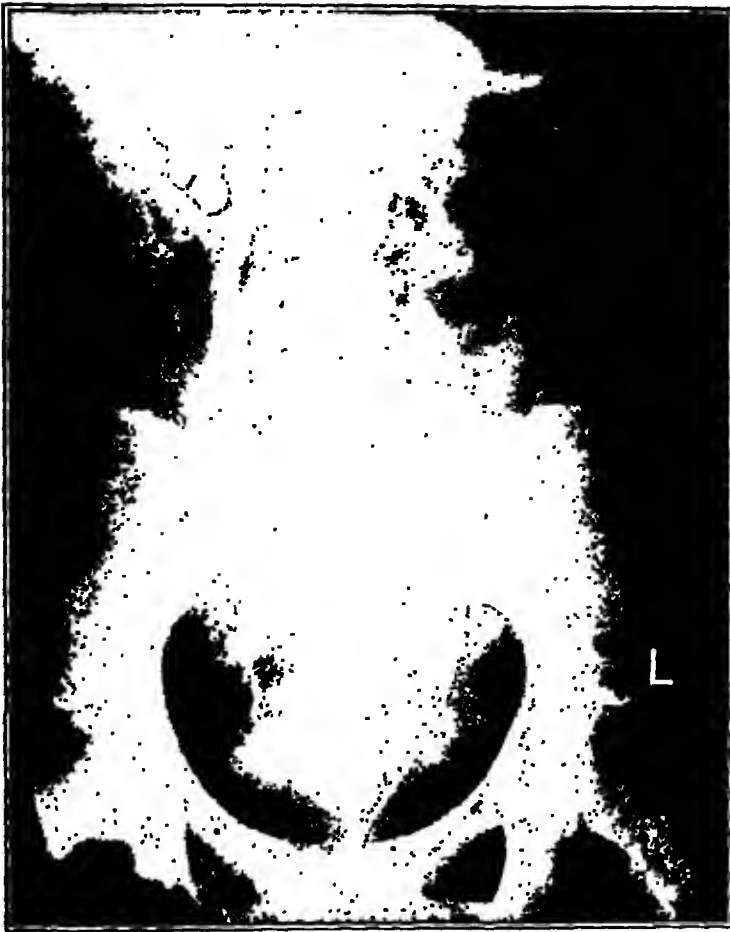


Fig. 7 (case 7).—Right pyelo-ureterogram showing a dilatation of the ureter above the first sacral vertebra. The lower ureteral section is normal in outline. From a case of puerperal ureteropyelitis.

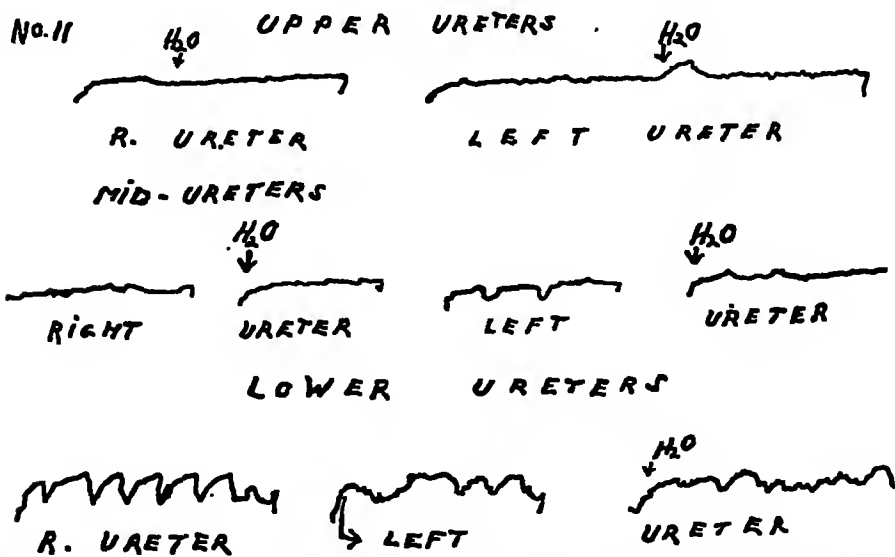


Fig. 8 (case 7).—Tracings from the upper, middle and lower sections of both sides showing activity only in the lower undilated portions of the ureters. There is atonia of the upper and middle sections and hypotonus of the lower sections.

dilatation of mid and upper ureters, also bilateral renal pelvic dilatation. The lower ureters, however, appeared normal in size.

Manometric tracing taken from the upper, mid and lower ureters on the right and left sides showed the absence of peristaltic activity in the mid and upper portions, while the lower undilated sections still had some contractile power, though they were hypotonic (figs. 7 and 8). The left pyelo-ureterogram was similar to that of the right side in appearance.

It is known that every portion of the excised ureter is capable of independent contractions. This case demonstrates that this may also be true of the intact unexposed ureter.

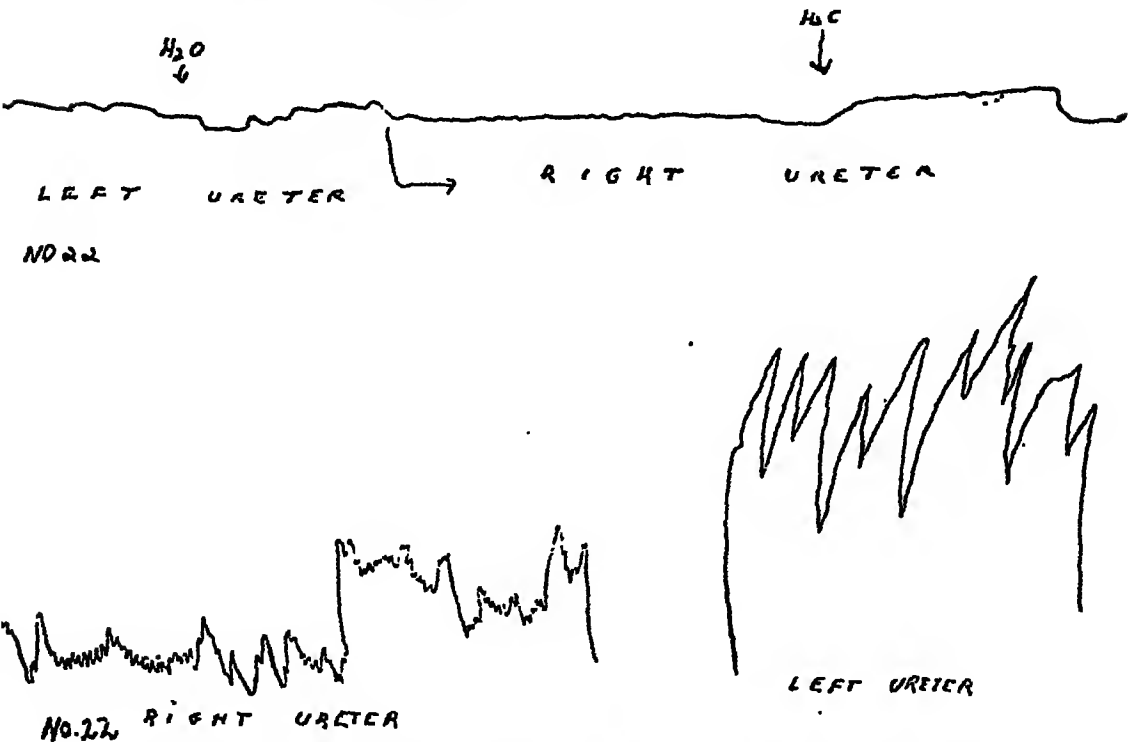


Fig. 6 (case 6).—The top tracing shows atonia of both ureters. The lower tracing (taken one week later) shows a recovery of activity on both sides.

CASE 8.—C. K., a woman, aged 35, complained of abdominal pain on the right side radiating to the back and groin. The pain was more severe when lying down than when being up and around, and also immediately prior to menstruation. There was dysuria, frequency and hematuria. A right pyelo-ureterogram showed a dilatation of the ureter and renal pelvis. Nine months later, a repeat pyelo-ureterogram showed the ureter restored to a normal caliber and the pelvis not so markedly dilated. Even though this is true, the manometric tracing taken at this time showed the right ureter to have only pendulum movements, there being no motor response to water. The pressure produced by manual compression of the kidney was repeatedly transmitted to the manometer, thus showing that the right ureter was still atonic and relaxed. The left ureter possessed spontaneous peristaltic waves (figs. 9, 10 and 11).

**CASE 9.**—L. B., a woman, aged 20, emaciated, had a condition clinically diagnosed: ureteropyelitis and peri-ureteritis. She complained of fever, pain in the right part of the back, loss of weight and frequency of urination of five weeks' duration.

On examination, tenderness was found in the right side of the lower part of the abdomen and right renal region. Cystoscopic examination revealed a bilateral infection (gram-positive cocci). Many white blood cells were found in specimens from both sides. The catheter passed on the right side, met an obstruction 17 cm. up on one occasion (verified by ureterogram), and on another occasion, no obstruction was encountered (also verified by pyelo-ureterogram).

Manometric tracing showed bilateral loss of ureteral activity. Two months later, after the patient had been relieved of her symptoms and pelvic lavage with mild silver protein given, the tracing showed the right ureter to have recovered a slight amount of activity, and the left ureter to have completely recovered its contractile power.

**CASE 10.**—A. P., a woman, aged 24, single, complained of chills, fever and pains in the back. For the past four or five years, she had had attacks of abdominal and lumbar pain at the menstrual period. As a child, she had been a bed wetter.

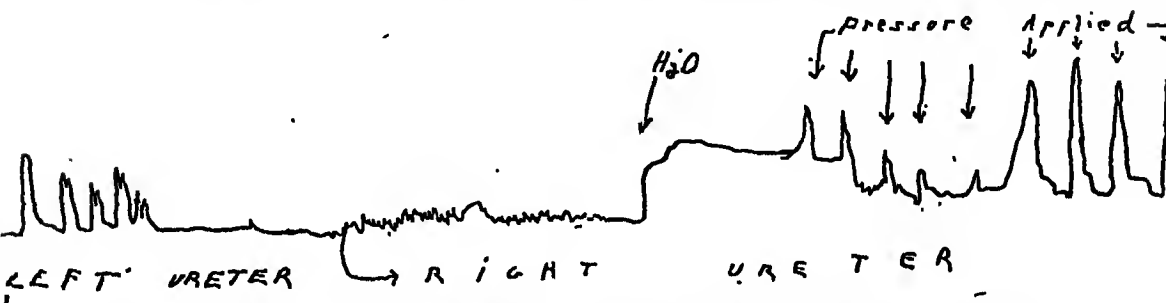


Fig. 11 (case 8).—Second degree ureteritis. Tracing, taken at the time of the last pyelo-ureterogram (which appears normal) shows the right ureter to be atonic and relaxed throughout, since pressure applied to the kidney is transmitted to the manometer.

The temperature was 104 F.; the urine contained many white blood cells. On examination, tenderness was noted over the right and left kidneys and along the course of both ureters, particularly the left. Both ureters were palpable and tender on vaginal examination. A left pyelo-ureterogram showed an absence of fluid in the lower section of the ureter; otherwise it was normal.

A clinical diagnosis was made of acute ureteropyelitis superimposed on a chronic ureteritis. Manometric tracings taken on three different occasions showed hypotonicity of both ureters and practically no response to intra-ureteral injections of water.

**CASE 11.**—A. W., a woman, aged 35, complained of dysuria and dull abdominal pain radiating into the groin and pain in the back, particularly on the left side. The pain was more acute during menstruation. She had had this trouble for the past ten years. A pelvic operation was done four years before without relief. On examination, tenderness was found along the entire course of the left ureter and in the left renal region. The right ureter was thickened and tender on vaginal examination. The left ureter was not palpable, but there was tenderness to light pressure in that region. Urinalysis was negative. Nothing abnormal was found on cystoscopic examination. A bilateral pyelo-ureterogram appeared normal.



Fig. 9 (case 8).—Right pyelo-ureterogram showing a moderate dilatation of ureter and pelvis.



Fig. 10 (case 8).—Pyelo-ureterogram, taken nine months later, showing a restoration of the ureter to a normal caliber.



CASE 14.—C. U., had tuberculosis of the right kidney with extensive ureteral involvement. The right ureter was palpable vaginally. Manometric tracing did not show any activity of the right ureter, there being no motor response to intra-ureteral injections of saline. The left ureter possessed some peristaltic activity.

Right nephro-ureterectomy was performed. The ureteral specimen showed extensive infiltration. The right pyelo-ureterogram did not show the degree of involvement actually present (figs. 12, 13 and 14).



Fig. 12 (case 14).—Tuberculosis of the kidney with ureteral involvement. Right pyelo-ureterogram. The pelvic and renal portions are typical of tuberculosis, while the outline of the ureter did not reveal the extensiveness of ureteral involvement found at operation.

CASE 15.—W. D., had left tuberculous pyonephrosis with extensive ureteral involvement. Manometric tracing did not show any spontaneous activity of the left ureter, and after two intra-ureteral injections of saline, there were pendulum but no peristaltic waves. The right ureter showed little spontaneous activity, but there was a peristaltic response to the intra-ureteral injection of saline. Left nephrectomy was performed. The ureter, as far as it could be seen at operation, was extensively infiltrated but could not be removed because of marked adhesions.

Manometric tracing showed a tendency to increased peristaltic activity on the left side, while hypotonus was found on the right side, there being no response to the intra-ureteral injection of water.

A diagnosis of ureteritis of second degree on the right side and first degree ureteritis on the left (?) was made.

NOTE: It is interesting to note that the patient complained of pain on the left side even though examination shows more involvement of the right ureter.

CASE 12.—E. H., a woman, aged 19, with puerperal pyelitis, seventeen days after normal delivery, full term pregnancy, had a temperature rising to 39 C. (102.2 F.), accompanied by marked tenderness over the right renal region, also some tenderness over the left renal area. The urine contained many white blood cells. The ureters were palpable on vaginal examination; the left felt thicker than the right.

Cystoscopic examination showed +++ white blood cells in urine from the left side and ++ white blood cells in urine from the right side. There was staphylococcus infection. Pyelograms were not made. Manometric tracing showed a complete abolition of activity of the left ureter and a diminution of activity of the right ureter. It is of interest to note that the patient complained of pain on the side that examination shows to be the least involved.

CASE 13.—V. C., a girl, aged 16, complained of pain in the back and lower part of the abdomen, dizziness and nausea. The patient stated that this trouble began one year before, immediately after her first intercourse. Menstruation occurred twice a month, the flow lasting for eight days. On examination, tenderness was found in both lumbar regions. On vaginal examination, there was tenderness along the course of both ureters, but they were not palpable.

Cystoscopic observations showed nothing abnormal. Manometric tracing showed inactivity of both ureters. Tracing repeated two weeks later, showed recovery of activity of both ureters. At this time the patient feels well and is symptomless.

Often it is rather difficult to make a dogmatic classification of some of the cases, since a late second degree ureteritis may belong to that of the third degree. It is unusual for recovery of activity to occur in the latter division, but it is possible in some instances, particularly in some cases of ureteropyelitis of pregnancy in which extreme ureteral dilatation is present, and after a year or longer the ureter may recover its normal caliber and activity.

#### *Third Degree Ureteritis.—Paralysis.*

Cases belonging to this division are those in which peristaltic ureteral activity has been permanently abolished because of extensive inflammatory infiltration (fibrosis) or because of thinning of the muscular coats by marked dilatation (atrophy). On vaginal examination, the ureter is found to be thickened in most instances, and there may or may not be tenderness to palpation. The manometric tracing shows complete absence of peristaltic activity, there being no response to intra-ureteral injections of fluid. Cases 14 and 15 are illustrative of cases in which tuberculosis of the kidney with ureteral involvement occurs.

activity spontaneously, nor any response to intra-ureteral injections of water or saline (figs. 17 and 18).

CASE 18.—F. F., had left renal lithiasis. Manometric tracings taken on two different occasions did not show any activity of the left ureter, spontaneously or



Fig. 15 (case 16).—Tuberculosis of the kidney without ureteral involvement. Left pyelo-ureterogram. The pyelogram is typical of tuberculosis of the kidney; the ureterogram shows some dilatation and a suspicion of the presence of ureteral involvement.

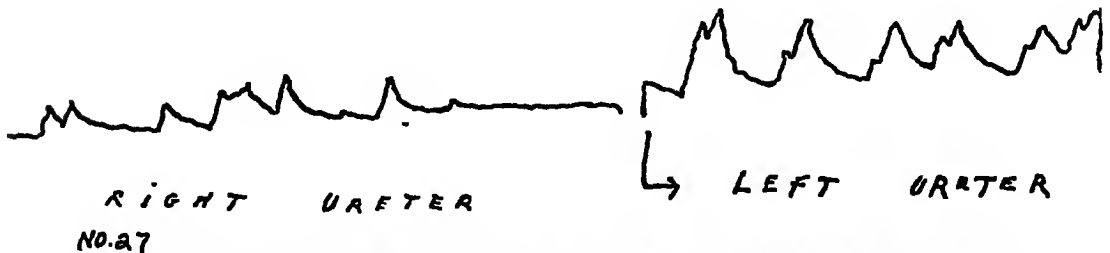


Fig. 16 (case 16).—Tracing showing both ureters to possess peristaltic activity. The operative specimen did not show any evidence of ureteral involvement.

after the intra-ureteral injection of water. The right ureter had pendulum movements, and a low grade of peristaltic activity, there being only a feeble response to the injection of water on this side.

Case 16 is illustrative of a case of tuberculosis of kidney without ureteral involvement.

CASE 16.—E. H., had tuberculosis of the left kidney without ureteral involvement. Manometric tracing showed both ureters to possess peristaltic activity. Left nephro-ureterectomy was performed. The ureter looked and felt normal (figs. 15 and 16).



Fig. 13 (case 14).—Operative specimen showing extensive ureteral infiltration.

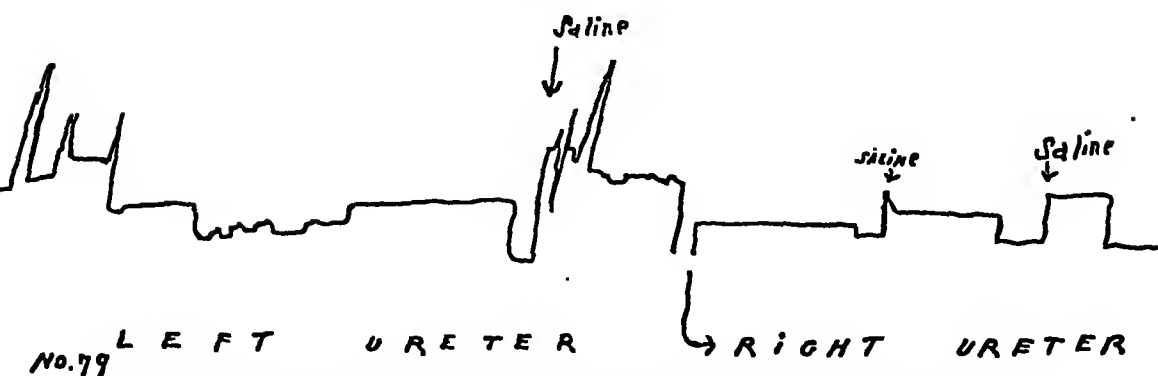


Fig. 14 (case 14).—Third degree ureteritis. Tracing from the right ureter shows a complete absence of peristalsis. The left ureter possesses spontaneous activity.

Cases 17, 18, 19, 20 and 21 are illustrative of cases of lithiasis in which manometric tracings are made.

CASE 17.—M. F., had multiple stones in the left kidney and a left lumbar fistula. Left nephrectomy was performed. Manometric record showed the right ureter to possess normal peristaltic activity. The left ureter did not show any

Left nephro-ureterectomy was performed. The left ureter was found to be markedly infiltrated. The patient died. The right ureter was removed at autopsy and was found to be the seat of early infiltration. The left pyelo-ureterogram did not reveal the extensive ureteral involvement found (figs. 19, 20 and 21).

CASE 19.—H. E., had bilateral ureteral stones and a right perirenal abscess. Manometric tracings showed bilateral atonia. Two days later (after a stone on the left side had passed) the pressure tracing showed a hypotonic left ureter and atonia of the right ureter.



Fig. 19 (case 18).—Renal lithiasis with infection. Extensive ureteral infiltration on one side, early infiltration on the other. The right pyelo-ureterogram shows moderate pelvic and ureteral dilatation. In the area of the left kidney there is a large shadow which is that of calculi.

CASE 20.—N. S., had stricture (which has been dilated) of the left lower ureter following ureterolithotomy performed three and one half months previously. At operation, the ureter appeared and felt normal; afterward there was wound infection communicating with the ureter. The left pyelo-ureterogram appeared normal, and the infection had completely cleared up at the time the tracings were taken.

Manometric tracing showed both ureters to possess good peristaltic activity. It is of interest to note that ureteral activity was not permanently arrested, even though there had been a severe infection.



Fig. 17 (case 17).—Renal lithiasis with infection. Ureteral infiltration. The left ureterogram shows obstruction of the upper ureter and multiple stones in the left renal area.

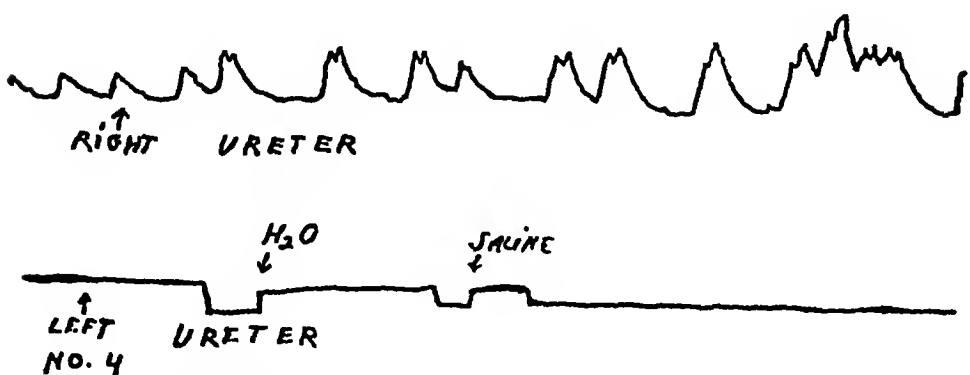


Fig. 18 (case 17).—Third degree ureteritis. The top tracing of the right ureter shows normal activity; the lower tracing is that from the left ureter and shows complete cessation of function.

CASE 21.—F. K., a man, aged 42, complained of severe pain (ureteral colic) on the left side. X-ray and cystoscopic examination showed a stone in the left lower ureter. A week later, the stone had passed spontaneously.

Manometric tracing (taken one week after the passage of the stone) showed the left ureter to have diminished contractile ability, and the right ureter to possess a normal peristalsis.

#### URETERAL DILATATION

The normal ureter is usually not patent throughout, for while it is in systole in one small segment, it is in diastole in another. It has been

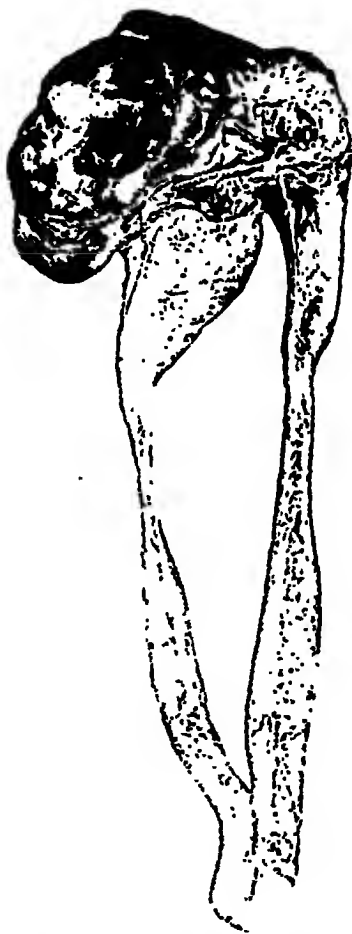


Fig. 22 (case 22).—Operative specimen. Kidney with double ureters. There is pelvic and ureteral dilatation.

found unusual for the pressure by bimanual compression of the kidney, or increased intra-abdominal pressure to be transmitted to the manometer through a hypertonic or normal ureter. If the pressure is transmitted, the ureter is either relaxed throughout momentarily or is atonic without dilatation, or there is dilatation without complete mechanical obstruction. The manometric tracing together with the pyelo-ureterogram furnishes complete data in regard to this. In some of the cases a tentative diagnosis of hydro-ureter was made and confirmed by the pyelo-ureterogram (cases 22 and 23).



Fig. 20 (case 18).—Operative specimen showing a kidney with a large calculi and a markedly infiltrated ureter.

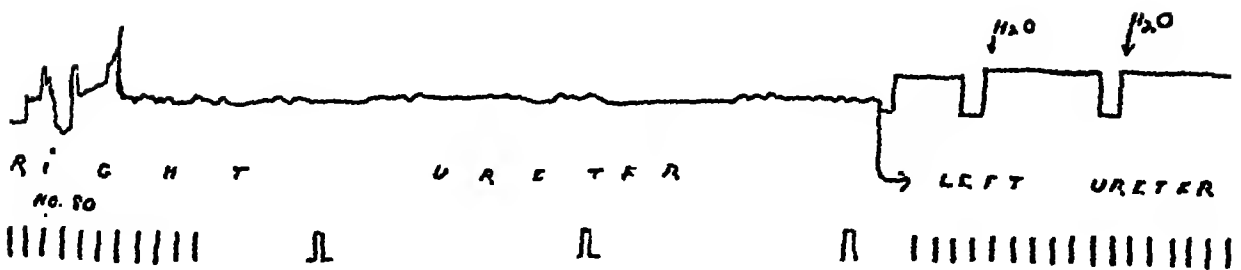


Fig. 21 (case 18).—Third degree ureteritis, left ureter; second degree ureteritis, right ureter. The tracing shows cessation of function of the left ureter and a low grade of activity of the right ureter.



activity could be demonstrated. Infection was absent in all. These were evidently early cases, but in those of long standing, particularly when associated with infection, hypotonus or paralysis of the ureteral musculature would, no doubt, be present.



Fig. 24 (case 26).—Autopsy specimen of kidney, ureter and bladder. There is a diffuse fibrosis with shortening of the ureter. There are perforating ulcers in the lower ureter. See figure 3 *D* for manometric tracing from this ureter.

#### THE MANOMETRIC TRACING AND THE PYELO-URETEROGRAM

Frequently evidence of ureteral involvement is not discernible from the plates, made after injections of opaque solution, even though it is known that such probably exists. This is particularly true of ureteritis

CASE 22.—G. N., had right hydronephrosis and hydro-ureter. Manometric tracing showed a complete absence of activity of the right ureter, there being no motor response to the injection of water. Deep renal compression was transmitted to the manometer. A tentative diagnosis of dilated ureter was made and confirmed by pyelo-ureterogram and operation (figs. 22 and 23).

CASE 23.—J. R., a man, aged 43, had right hydronephrosis and hydro-ureter (infected, renal calculi).

Manometric tracing showed that the right ureter had no spontaneous activity and that there was no motor response to the injection of water, while the left ureter had a normal peristaltic activity. Pressure produced by bimanual compression of the right kidney can be repeatedly transmitted to the manometer. The foregoing diagnosis, made tentatively, was confirmed by the pyelo-ureterogram and operation.

CASE 24.—G. M., had puerperal ureteropyelitis. Pyelo-ureterograms showed marked bilateral ureteral dilatation with kinking of the middle of the left ureter. Manometric tracings, taken on two different occasions, showed both ureters to be without peristaltic activity, there being no motor responses to the injection of water. Pressure, produced by bimanual renal compression was transmitted to the manometer on the right side, but because of the presence of a ureteral kink there was no transmission of pressure on the left side.

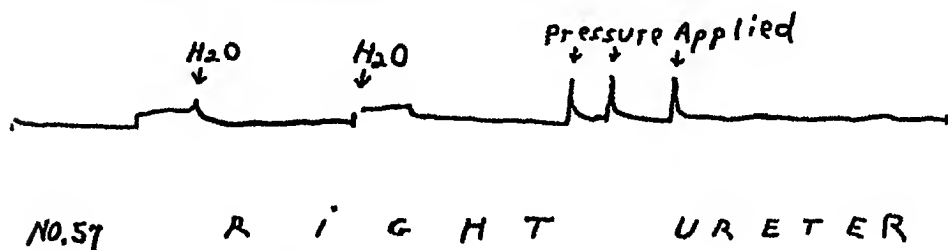


Fig. 23 (case 22).—Tracing showing inability of the ureter to contract. Pressure produced by bimanual compression of the kidney is transmitted to the manometer. Because of this, a tentative diagnosis of dilated or relaxed ureter was made and confirmed. It is not known from which ureter the tracing was taken.

CASE 25.—M. B., had carcinoma of the cervix with extension and compression of the right lower ureter. There was a moderate dilatation of the ureter and pelvis above the obstructed area.

Manometric tracing showed a complete absence of activity of the right ureter, there being no motor response to water injection, while the left ureter has spontaneous peristaltic activity.

Case 26 is illustrative of one in which diffuse fibrosis occurred.

CASE 26.—A. C., a woman, aged 39, had diffuse fibrosis of the ureter and perinephritic abscess. Manometric tracing of the right ureter did not show any peristaltic activity, there being no motor response to injections of water (figs. 24 and 3D).

#### PERISTALTIC ACTIVITY IN THE PRESENCE OF CORD BLADDER

Three patients were examined, one having syphilitic transverse myelitis, the other two having tabes. No interference with ureteral

6. The manometric tracings allow classification of ureteritis into three varieties according to the degree of ureteral activity.

7. That the manometric tracings represent the actual conditions of the ureter has been confirmed in some instances by the gross and microscopic examination of the specimen and in other instances by plates made following injections with opaque solution.

8. Relief of symptoms in patients who have ureteritis or ureteropyelitis appears to occur simultaneously with the recovery of ureteral activity. Aggravation of the disease, however, seems to be concomitant either with ureteral hyperactivity or with the loss of peristaltic contractile ability.

9. Mechanical ureteral obstruction cannot be dissociated from functional ureteral impairment, but there may be loss of function in the absence of mechanical interference.

10. The impression that the method is completely efficient in diagnosis should not be obtained. It is intended as an additional aid, and I hope that as the polygraph and electrocardiograph have been valuable adjuncts in the study of circulatory disturbances, so the recording of ureteral peristalsis will prove to be a useful and valuable method in the study and diagnosis of renal pelvic and ureteral disease.

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of the first and second degree, while in cases belonging to the third degree, the pyelo-ureterogram does not always reveal the true extent of involvement. Given a normal pyelo-ureterogram, this does not necessarily mean that the pelvis and ureter function normally. Given a moderate ureteral dilatation or a low lying kidney with ureteral displacement; this does not necessarily mean ureteral incompetency. Case 8 (figs. 9, 10 and 11) demonstrates that manometric tracing depicted the state of the ureter more accurately than did the pyelo-ureterogram.

The disturbances of ureteral function and the degree of same appear to be accurately shown by the manometric tracings, and frequently long before the changes would be obvious enough to be discovered on the x-ray plates. That the manometric observations represent the actual condition of the ureter has been corroborated, in some instances when it was possible, by the gross and microscopic examination of the specimen, and in other instances by the pyelo-ureterographic observations.

The tracings have been of aid in the interpretation of the studies made following injections of opaque solution, and in deciding which side to pyelograph when there appears to be no difference on either side from the various other examinations.

#### CONCLUSIONS

1. A more sensitive instrument, which is adaptable to the clinic as well as to the experimental laboratory, is presented for the recording of ureteral peristalsis.

2. The ureter possesses two chief types of contractions, the waves of which assume various configurations. There are also tonus variations and changes of rhythm.

3. The rôle of congestion of the female ureter in simple ureteritis is discussed.

4. Manometric tracings have been taken in the following conditions: (a) normal; (b) hydro-ureter and hydronephrosis; (c) lithiasis; (d) after uretero-lithotomy, and after the spontaneous passage of ureteral stone; (e) cord bladder; (f) bilateral complete duplication of ureters—simultaneous records of all ureters, and (g) ureteritis of various degree: tuberculous and nontuberculous.

5. Manometric tracings are of clinical value in detecting early as well as late disturbances of ureteral function; in the assistance in the diagnosis of dilated ureter and pelvis without opaque studies, or to supplement the latter; in deciding which ureter to inject with opaque solution when there appears to be no difference on both sides from the various other examinations; in knowing whether the ureter is involved in tuberculosis, calculous disease, tumor, etc.

# THE EFFECT OF SOLUTIONS OF PITUITARY AND VARIOUS DRUGS ON THE MOVEMENTS OF THE SMALL INTESTINE DURING SIMPLE MECHANICAL OBSTRUCTION \*

C. A. McINTOSH, M.D.

William Stewart Halsted Fellow in Surgery

AND

J. C. OWINGS, M.D.

BALTIMORE

While investigating the degree of intra-intestinal pressure in simple obstruction,<sup>1</sup> a method was employed which was thought to give a fairly exact conception of the type and magnitude of the intestinal motility. The degree of pressure was found to be maintained at a level (from 6 to 8 cm. of water) about twice that of the normal maximum (from 2 to 4 cm. of water), and when the intestine became active, the pressure rose to ten or fifteen times the normal (from 30 to 60 cm. of water). Having determined the type of motor activity and the degree of intra-intestinal pressure in this condition, it was concluded to record the effect of certain tissue extracts and drugs on the movements of obstructed intestine and on the intra-intestinal pressure..

For the most part, the action of a drug on smooth muscle, such as is found in the intestine, is usually determined by a suspension of a slip of that muscle in a water-bath and the addition of the drug to the medium. Perhaps the best example of this is in the biologic assay of solution of pituitary when the suspended uterus of a virgin guinea-pig is employed. In such studies it must be appreciated that certain factors and abnormalities are introduced which either are not present or might materially alter the effect of the same drug on that tissue when it is given to the living animal. Some of these factors are the contents of the medium, changes in temperature, acid-base equilibrium, the approach of the drug to the tissue, nervous control, both local and central, and nutritional abnormalities. Experiments that are conducted on a living animal eliminate many of these abnormalities, and perhaps the practical value and extent of activity of any drug or tissue

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\* From the Department of Surgery, Hunterian Laboratory, The Johns Hopkins University.

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#### ABSTRACT OF DISCUSSION

DR. W. F. BRAASEN, Rochester, Minn.: The physiologic studies which were made of the ureter by Dr. Trattner are exceedingly interesting and should prove to be of practical value. I am glad that my view of the atonic or inflammatory ureter which I have held many years based on clinical and urographic evidence is confirmed by recent investigations. We are realizing more and more the importance of this pathologic change in the ureter, and when present it will affect our treatment to a marked degree.

DR. PAUL W. ASCHNER, New York: Dr. Trattner's studies on the ureter will prove most important. I do not know whether he correlates his tracings with his pyelographic study. We have always given our patients indigo carmine (sodium indigolindisulphonas) and have noticed for a number of years that in a considerable number of patients with hydro-ureter and hydronephrosis there was a marked difference in the type of ejaculation from the ureter as it came out stained with the indigo carmine. We have found that on the diseased side there is much less direct ejaculation, the fluid rather seeping out. We have had one patient under observation for a number of years, who, following pregnancy, was left with a persistent, painful, dilated kidney and ureter which, on every examination, show this phenomenon. In spite of all treatment, this has persisted. In other words, evidence of disturbance of the function of ureteral musculature can be discovered by chromoscopy.

confirm these same observations. Degener,<sup>12</sup> in investigating the effect of dried on the hypophysis of the albino rat, maintained that while the nervous portion causes a relaxation of the isolated intestinal slip, the glandular portion causes a contraction, and while the whole gland gives chiefly relaxation, after feeding with oatmeal and a vegetable diet, the total extract from the hypophysis causes contraction. Uno,<sup>13</sup> also working with albino rats, found that extract of the hypophysis, after the animals had been fighting for from one to six hours, caused a contraction of the intestinal slip as contrasted with the extract from the control gland, which gave relaxation. Dixon,<sup>14</sup> working on cats and dogs, noted that injections of solution of pituitary increase the tone of the small intestine but decrease the tone in the large bowel.

Perhaps the first observation of a typical inhibitory response of isolated intestine to solution of pituitary was made by Bayer and Peter,<sup>15</sup> in 1911, while working with pituitrin prepared by the Parke, Davis Company. They also sometimes observed increased activity after the period of inhibition. It must be borne in mind, too, that Blair Bell, in 1909, in testing suspended loops of intestine in Ringer's solution, found that the addition of infundibular extracts caused a relaxation and cessation of movement, but that often this was preceded by a powerful contraction.

In 1916, Shamoff<sup>16</sup> found that certain preparations from the posterior lobe resemble extracts of the suprarenal medulla in that they produce relaxation of the isolated intestinal loop and inhibition of its rhythmic contractions. Hoskins<sup>17</sup> observed relaxation of the dog's intestines when pituitrin was injected intravenously. Pancoast and Hopkins<sup>18</sup> made x-ray studies of eleven patients after giving pituitrin. They reported a primary depressing influence in the stomach on peristalsis, motility or both, followed by an increase of both. In the small intestine the motility, as a rule, was not affected or was slightly delayed. In the large bowel little if any effect was noted.

Atwell and Marinus<sup>19</sup> observed an inhibition of the intestinal rhythm of the isolated intestinal segment of the rabbit by rather weak dilutions of solutions of pituitary. Strong solutions, they stated, increase the activity.

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12. Degener: *Am. J. Physiol.* 60:118, 1922.

13. Uno: *Am. J. Physiol.* 61:208, 1922.

14. Dixon: *J. Physiol.* 57:136, 1923.

15. Bayer and Peter: *Arch. f. exper. Path. u. Pharmacol.* 64:204, 1911.

16. Shamoff: *Am. J. Physiol.* 39:253, 1916.

17. Hoskins, R. G.: *Pituitary Extract*, *J. A. M. A.* 66:733 (March 4) 1916.

18. Pancoast and Hopkins: *New York M. J.* 105:289, 1917.

19. Atwell and Marinus: *Am. J. Physiol.* 47:76, 1918.

extract may be more truthfully observed. Again, a correction must occasionally be made for species, and in this connection it must be stated that all the following observations were made on the dog.

Other methods of determining the motor response of the intestine to certain drugs have been by means of x-ray, direct observation of the exposed intestine, the rubber balloon method and by alteration in the rate of discharge of the intestinal contents. In all of these methods some degree of error is introduced, and each has its limitations; so, too, in the method to be described certain abnormalities are introduced and difficulties encountered. These, in the main, will be found to consist of the following: the necessity of inducing a simple mechanical intestinal obstruction, which necessitates an anesthetic and laparotomy, and the introduction of a foreign body into the lumen of the intestine. On the other hand, one is eventually able to procure what we consider good graphic records of the intestinal motility, while the degree of intra-intestinal pressure may be ascertained with a fair degree of accuracy.

The method of preparing the animals for these observations has been already described, but a repetition may be given here in brief.

#### TECHNIC

All animals were given  $\frac{1}{4}$  grain (0.016 Gm.) of morphine hypodermically and ether anesthesia before operation. In some instances procaine, 2 per cent, was used locally. Strict aseptic precautions were employed. The bowel was doubly clamped about 6 inches (15.2 cm.) above the ileocecal valve and cut across. The lower end was turned in by the Parker-Kerr method and reinforced by a double row of mattress sutures. The clamp was removed from the proximal portion of the bowel and its lumen opened, into which was placed the following apparatus: It consisted of a brass tube about 2 inches (5.08 cm.) long, with an internal diameter of 3 mm. and a threaded external surface. A concave metal disk about 1.5 cm. in diameter was fixed at one end and a



line on the tracings, not one instance of increased motor activity was found. In every case, the graphic record is a straight line that tends to approach the base line, indicating a falling off of intra-intestinal pressure and tone, and the absence of motor activity. The duration of these effects is dependent on the quantity of pituitary fluid given. The largest doses, 0.5 or 1 cc., are effective for from twenty to thirty minutes, while the smaller ones, 0.025 or 0.05, act for only from five to ten minutes at the most. The general constitutional reaction seems to go hand in hand with the effect on the obstructed intestine. When the one has passed off and is finished, the other, too, is returned practically to the same condition as before the injection. Or if the effects of the drug are delayed, as following the intramuscular injection, in the same way the response in the bowel occurs at the same time as the general reaction.

In a few instances, it has been possible to observe intense peristaltic activity through a thin and scaphoid abdomen. When this was the case, or when the same could be induced by giving eserine, and much gurgling could be heard, the giving of a moderate quantity of pituitary fluid would cause a disappearance of the visible peristalsis and a cessation of the noises.

Besides pituitary fluid and pituitrin, we have tried the effect of two other extracts of the posterior lobe of the pituitary gland, known as vasopressin and oxytocin. These preparations were procured from a batch that had been sent out by the Parke, Davis Company for clinical use and experimental trial. Kamm<sup>21</sup> and others have indicated their method of preparation and have brought forward good evidence to show that these substances represent two principles that are present in the posterior lobe of the hypophysis.

Though, as is shown in table 1, we have made only five injections, three with oxytocin and two with vasopressin, we have noted practically the same results as we have experienced with solution of pituitary and pituitrin, except for the following differences: The vasopressin would appear to possess a pressor substance in much greater concentration than in pituitary fluid, pituitrin or oxytocin, for an intravenous injection of 0.25 cc. caused an extreme blanching of the mucous membranes and fall in the pulse rate that were much more marked than was ever noted with 1 cc. of the other substances. Oxytocin gave the same constitutional reaction and effect on the intestinal motility as did pituitary fluid or pituitrin.

As such a constant and definite result was observed after each injection of pituitary fluid, and this contrary to what was considered

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21. Kamm, Aldrich, Grote, Rowe and Bugbee: *J. Am. Chem. Soc.* 1:573, 1928.

Recently, McDonald<sup>20</sup> threw great doubt on the commonly held view that the pituitary gland contains a general stimulant of plain muscle fibers. He believes that solutions of pituitary vary greatly in their content of intestinal stimulant; that this intestinal stimulant is alcohol-soluble and alkali-stable, and that the pituitary gland is not essentially richer in the stimulant than are several other tissues.

The studies that we have made on the effects of solution of pituitary on the intestinal motility have been carried on for the most part with one preparation. The powder from which this pituitary liquid was made was prepared according to the directions given in the tenth revision of the U. S. P. except that it was subjected to an additional seventy-two hour extraction with absolute alcohol in a Soxhlet apparatus. The solution, containing 5 mg. of powder per cubic centimeter, was made up freshly each day. The additional extraction was done in the laboratory of the pharmacological department of the Johns Hopkins University School of Medicine and the solution made through the kindness of Dr. Geiling.

A number of tests were made with pituitrin prepared by the Parke, Davis Company, and the effects of this drug, so far as intestinal motility is concerned, are identical with those procured when our own freshly made pituitary fluid was used.

As already mentioned, a good record of the intestinal motility may be procured by the foregoing method from thirty-six to forty-eight hours following the establishment of simple obstruction. Any time after this, injections of pituitary fluid may be given, intravenously and intramuscularly, and the results noted. Coincident with the effects seen on the motility of the bowel, certain general constitutional reactions were observed that in a sense confirmed that the extract was active. These in the main consisted of a marked slowing of the pulse rate and respirations, an extreme degree of blanching of the skin and mucous membranes; if the dose was sufficiently large, the animal became "knocked out" as it were, and lay extremely still if it had been active previously. These responses following intravenous injection came on instantaneously, while after intramuscular injections, the constitutional responses were delayed from three to ten minutes.

As will be seen in the accompanying tables, the doses varied from 0.025 to 1 cc., the former being about as small an amount as could be given and still furnish positive and definite general effects. In every instance, as shown by a large number of graphic records, the response of the obstructed small intestine was the same. Whether the bowel was in an extreme state of motor activity, either spontaneous or induced, as the result of stimulation from some drug such as eserine, or whether the intestines were inactive, as would be shown by a straight

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20. McDonald: *Quart. J. Exper. Physiol.* 15:191, 1925.

TABLE 1.—*Effect of Pituitary Fluid and Pituitary on Intra-Intestinal Pressure During Obstruction of the Small Bowel; Concomitant Systemic Effects—Continued*

Series Number	Dog	Hours Obstructed	Drug	Quantity, Cc.	Method of Injection	Maximal Intra-Intestinal Pressure, Cm. Water		Pulse Rate		Pallor of Mucous Membrane	Duration of Effect, Minutes
						Before	After	Before	After		
OP 34	166		Pituitary fluid	0.025	Intravenously	16-18	6-8	180	123	Slight	7
OP 34	167		Pituitary fluid	0.025	Intravenously	30	8-10	180	148	Slight	10
OP 34	168		Pituitary fluid	0.025	Intravenously	26-28	26-28	184	180	Slight	..
OP 33	96		Oxytocin	0.5	Intravenously	18	6-8	...	Slowing	Moderate	15
OP 36	47		Oxytocin	0.5	Intravenously	32	2-4	144	92	Marked	30+
OP 36	47½		Oxytocin	0.4	Intravenously	2-4	2-4	132	92	Marked	20+
OP 36	51		Vasopressin	0.25	Intravenously	30	4-6	132	56	Extreme	50
OP 36	52		Vasopressin	0.25	Intravenously	3-4	3-4	120	64	Extreme	20+

the general belief concerning the mode and manner of action of this substance, we attempted a few experiments to determine the action of pituitrin and solution of pituitary on the isolated strip of a dog's intestine. In selecting portions of bowel for these studies, we have been well aware of the variety of conditions to which they were subjected. For example, we have used portions of intestine that have been obstructed from forty-eight to ninety-six hours. We have also employed bits of bowel that were procured from dogs that died almost instantaneously from thoracotomy and bleeding. Practically all the material obtained in this manner was kept, after thorough washing, in freshly made Locke's solution according to the modification of Smith and McClosky.<sup>22</sup> In other cases, absolutely fresh material was cut off as required from the intestine of an animal kept under iso-amyl-ethyl anesthesia, thus preventing any fall in temperature. Added to these variations, the slips of muscle suspended were cut in some cases longitudinally and in others transversely, in order to determine the effect on both types of muscle fiber.

The slips of muscle that were procured under these many and varied conditions were suspended in the usual manner in 100 cc. of freshly made Locke's solution, provided with an adequate supply of oxygen and kept at a constant temperature of 37 C. by a surrounding water-bath. The ordinary lever and kymograph completed the equipment.

The quantities of pituitary fluid, pituitrin and oxytocin added to the medium in which the muscle slips were suspended varied from 0.05 to 5 cc.; that is, from 0.25 to 25 mg. per cent of dry powder. In all instances, with the exception of two cases, and there were close

22. Smith and McClosky: U. S. Public Health Serv., Hyg. Lab. Bull., 1924, no. 138.

TABLE 1.—*Effect of Pituitary Fluid and Pituitary on Intra-Intestinal Pressure During Obstruction of the Small Bowel; Concomitant Systemic Effects*

Series Number	Dog	Hours Obstructed	Drug	Quantity, Cc.	Method of Injection	Maximal Intra-Intestinal Pressure, Cm. Water		Pulse Rate		Color of Mucous Membrane	Duration of Effect, Minutes
						Before	After	Before	After		
OP 27		6	Pituitary	1	Intra-venously	2-4	2-4	100	60	Extreme	25
OP 27		72	Pituitary	1	Intra-venously	2-5	2-5	...	...	Extreme	20
OP 27		126	Pituitary	1	Intra-venously	11	6-8	200	120	Extreme	25
OP 28		21	Pituitary	1	Intra-venously	6-8	2-4	...	...	Extreme	20
OP 28		72	Pituitary	1	Intra-venously	2-4	2-4	...	...	Extreme	20
OP 29		21	Pituitary	1	Intra-venously	11	2-4	...	...	Extreme	15
OP 29		4	Pituitary	1	Intra-venously	8-10	2-4	...	...	Extreme	20
OP 33		31	Pituitary	1	Intra-muscularly	18-20	2-4	100	60	Marked	50
OP 33		72	Pituitary	1	Intra-venously	28	4-6	...	...	Extreme	20
OP 33		76	Pituitary	1	Intra-muscularly	18	2-4	108	68	Moderate	60
OP 31		50	Pituitary	1	Intra-venously	32	4-6	...	...	Extreme	20
OP 31		68	Pituitary	1	Intra-muscularly	48	2-4	120	81	Moderate	15
OP 31		76	Pituitary	1	Intra-muscularly	21	4-6	110	72	Moderate	25
OP 27		121	Pituitary	0.5	Intra-venously	20	2-4	...	...	Marked	25
OP 27		126	Pituitary	0.5	Intra-venously	8-10	2-4	200	120	Marked	20
OP 27		137	Pituitary	0.5	Intra-venously	15	2-4	200	121	Marked	20
OP 27		45	Pituitary	0.5	Intra-muscularly	1-6	2-4	128	80	Moderate	20
OP 22		61	Pituitary	0.5	Intra-venously	21	4-6	...	...	Marked	20
OP 31		48	Pituitary	0.5	Intra-muscularly	18	6-8	121	68	Moderate	20
OP 31		56	Pituitary	0.5	Intra-venously	10-12	2-4	120	72	Marked	15
OP 31		57½	Pituitary	0.5	Intra-muscularly	18-20	2-4	121	81	Moderate	15
OP 23		56	Pituitary	0.25	Intra-venously	20	12	...	...	Moderate	20
OP 21		43	Pituitary	0.25	Intra-venously	25	6-8	...	...	Moderate	10
OP 23		66	Pituitary	0.1	Intra-venously	20	4-6	110	60	Moderate	12
OP 31		120	Pituitary	0.1	Intra-venously	10-12	2-4	120	68	Moderate	10
OP 31		126	Pituitary	0.1	Intra-venously	26	5-6	168	81	Moderate	10
OP 31		140	Pituitary	0.1	Intra-venously	6-8	4-6	...	...	Moderate	5
OP 23		120	Pituitary	0.05	Intra-venously	10-12	6-8	120	60	Slight	10
OP 23		120½	Pituitary	0.05	Intra-venously	10-12	6-8	128	72	Slight	10
OP 23		121	Pituitary	0.05	Intra-venously	10-12	6-8	108	66	Slight	15
OP 21		126	Pituitary	0.05	Intra-venously	48	8-10	168	81	Slight	5
OP 24		126½	Pituitary	0.05	Intra-venously	5-6	5-6	168	92	Slight	10
OP 23		141	Pituitary	0.025	Intra-venously	18-20	6-8	110	76	Slight	5
OP 23		144½	Pituitary	0.025	Intra-venously	16-18	2-4	126	72	Slight	5
OP 23		163	Pituitary	0.025	Intra-venously	10	5	148	96	Slight	5
OP 21		111	Pituitary	0.025	Intra-venously	4-6	6-8	150	112	Slight	5
OP 21		144½	Pituitary	0.025	Intra-venously	14-16	10-12	118	108	Slight	5
OP 21		149	Pituitary	0.025	Intra-venously	26-30	6-8	...	...	Slight	4

though its duration is somewhat shorter and not so pronounced, provided the quantity employed is the same in each instance. With small doses, still sufficient to give a constitutional effect, the repetition does not bring about continued inhibition of the intestinal motor activity, though certain constitutional effects still recur.

#### ESERINE

The action of eserine sulphate, as it is stated in the standard texts on pharmacology (Cushny,<sup>23</sup> Meyer and Gottlieb,<sup>24</sup> Poulsson<sup>25</sup> and others) is that of stimulation of both smooth and voluntary muscles either through their motor end-plates or through the production of a hypersensitivity of these same structures. Its employment, then, as a stimulant of bowel musculature is to be expected. Martzloff,<sup>26</sup> using the small dosage of 1/100 grain (0.00065 Gm.) together with 1/40 grain (0.0016 Gm.) of strychnine, reported that the clinical use of this

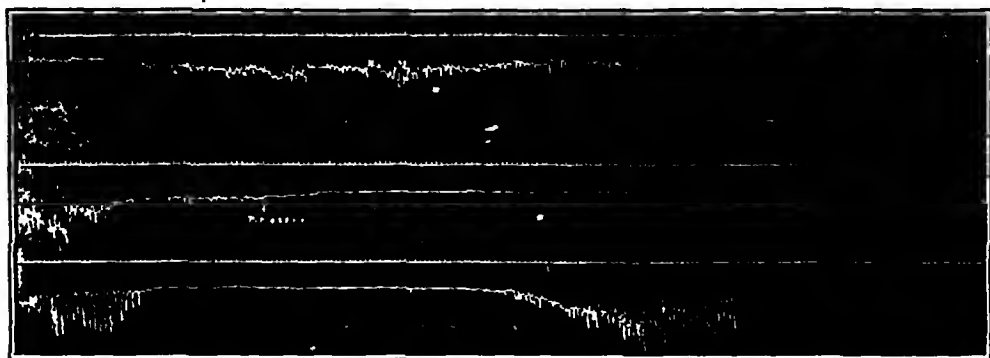


Fig. 4 (O. P. 34).—Record for dog obstructed for forty-three hours. The top tracing shows the normal; reaching a maximal intra-intestinal pressure of 24 cm. of water; the second tracing shows the effect of 0.25 cc. of pituitary fluid given intravenously. The bowel was inactive for ten minutes.

drug in the prevention of distention, and other conditions, was far from satisfactory. Martin and Weiss,<sup>27</sup> on the other hand, employing a much larger dose, from 1/16 to 1/20 grain (0.004 to 0.003 Gm.) of physostigmine salicylate, found satisfactory and beneficial results in those cases with a nontoxic type of distention. It was found less

23. Cushny: A Text Book of Pharmacology and Therapeutics, ed. 8, Philadelphia, Lea & Febiger, 1924.

24. Meyer and Gottlieb: Experimental Pharmacology as a Basis for Therapeutics, ed. 2, Philadelphia, J. B. Lippincott Co., 1926.

25. Poulsson: A Text Book of Pharmacology and Therapeutics, Baltimore, Williams & Wilkins Company, 1924.

26. Martzloff: Bull. Johns Hopkins Hosp. 35:370, 1924.

27. Martin, H. E., and Weiss, S.: Use of Physostigmine in Abdominal Distention, J. A. M. A. 84:1407 (May 9) 1925.

to one hundred fresh preparations, we found no stimulation, a fall in the tone or a cessation of the rhythmic movements. In the one there was a cessation of the rhythmic movements and a slight rise in the tone. In the other, a questionable stimulation occurred; that is, a slight increase in the height of one of the rhythmic waves was recorded, though from its appearance it would not seem unusual if



Fig. 2 (O. P. 33).—Record for dog obstructed for sixty-eight hours. The uppermost tracing is the normal with maximum pressure of 27 cm. of water; the second tracing was made following the injection of 1 cc. of pituitary fluid intravenously. The cessation of waves and the fall of pressure to 3 cm. of water should be noted. The lowest record shows a return of peristalsis after twenty-three minutes. A rise in the intra-intestinal pressure is represented in all the tracings by a descent of the graph toward the bottom of the record. The timer records every sixth second.

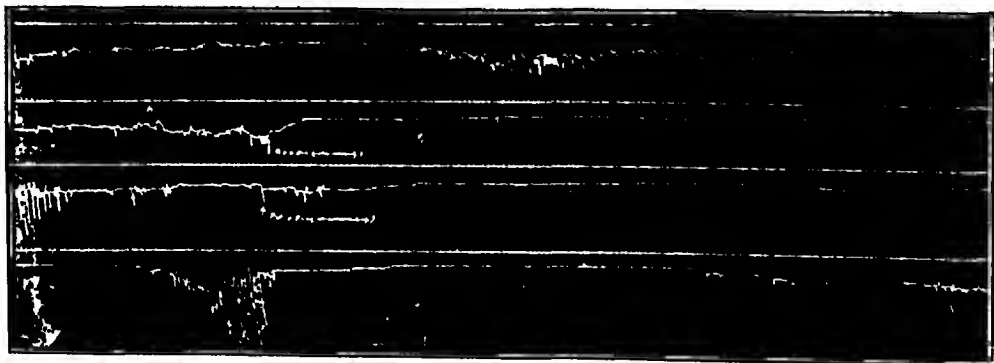


Fig. 3 (O. P. 34).—Record for dog obstructed for fifty-five hours. The top tracing shows the normal; the second, the effect of 0.5 cc. of pituitary fluid given intravenously. The third shows the return of motor activity after fifteen minutes when 0.5 cc. was given intramuscularly.

pituitary had not been added to the medium. The accompanying tracings show in a general way the results obtained.

Repeated doses of pituitary fluid or pituitrin in the animal with intestinal obstruction caused the same general constitutional reactions and the same effect in the intestinal motility as did the first injection,